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The Bulletin of the Association for the Study of Internal Secretions

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NEW EXPERIMENTAL DATA ON THE QUESTION OF THE SEAT OF THE ENDOCRINE FUNCTION OF THE TESTICLE.*

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The theory of Bouin and Ancel that the endocrine function of the testicle in mammals is mediated by the interstitial cells, grounded upon the extensive research of these authors, has been supported by Tandler and Grosz, Steinach, Sand and by myself.* But lately several attacks upon this theory have been made, especially by Kohn (1), Benda (2) and Stieve (3), without new experimental data having been added. These authors are of the opinion that only the generative part of the testicle has an endocrine function, the interstitial cells being a trophic organ for the former.

Different experiments performed by myself and my co-workers, *Wagner, Ottow, Bormann* and *Kropman*, during the past two years have enabled us to throw some light on certain aspects of the problem. In the following I will present a short account of the observations we have communicated in different places; some of them have not been previously published.

*The literature is reviewed in my book "Die Pubertätsdrüse und ihre Wirkungen." Berne, 1919.

2 SEAT OF ENDOCRINE FUNCTION OF TESTICLE

I.

Is a normal internal secretion of the testicle in mammals possible without fully developed interstitial cells? That this is not possible is shown by two of our experiments.

A. On a rabbit (4) (Prot. No. 4) about a month old one entire testicle and half of the second were removed. The animal was observed until the age of 8 months. The penis remained infantile. A small testicular fragment was found. That the

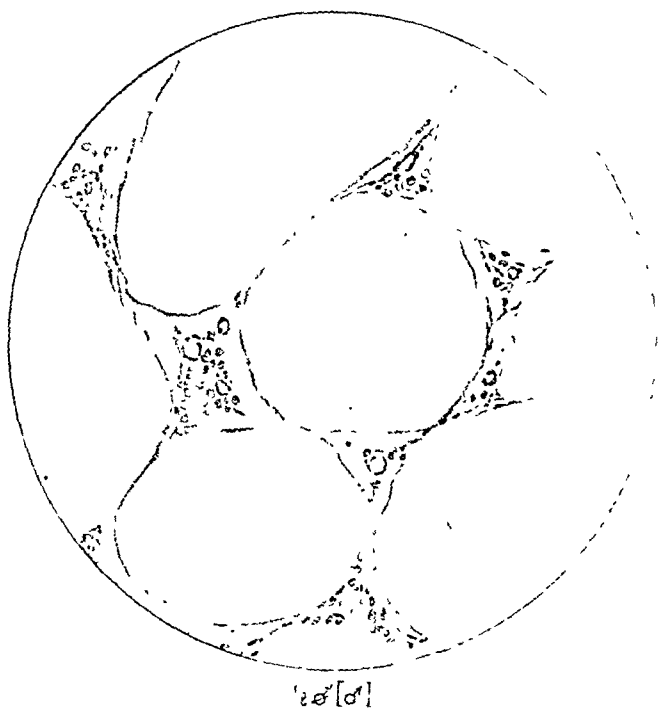


Fig. 1. Section through testicle of a rabbit 6½ months old, semicastrated at an age of 6 weeks. The animal had a normal penis. Interstitial cells with a large area of protoplasm around the nucleus. Seminiferous tubules in full spermatogenesis (not drawn). Fixation, Belly; Stain, Hem.-Eos. [All figures from preparations of Dr. Wagner, drawn by Miss L. Lebbert (except Fig. 3, drawn by Dr. Wagner) with the drawing apparatus of Leitz. Obj. Zeiss D. The scale is given in Fig. 6. All figures are reduced one-half.]

eunuchoidism of this animal was not caused by the fact that the quantity of testicular substance was too small, is shown by our numerous experiments on guinea pigs. In these animals extraordinarily small testicular fragments, representing only about 1 per cent of the weight of two normal testicles, were sufficient for the full development of the somatic sexual characters (5). The eunuchoidism in this experiment must have been caused by the underdevelopment of the testicular fragment as

shown by microscopical examination. The seminiferous tubules were somewhat further developed than in an animal of about two months, the diameter being greatly enlarged, and the quantity of cells, likely cells of Sertoli, being increased. Spermatogonia were present. Some tubules were filled with desquamated cells; it seems that these were cells of Sertoli surrounding spermatogonia. The intertubular tissue was richly developed, but consisted chiefly of common connective tissue. As far as interstitial cells

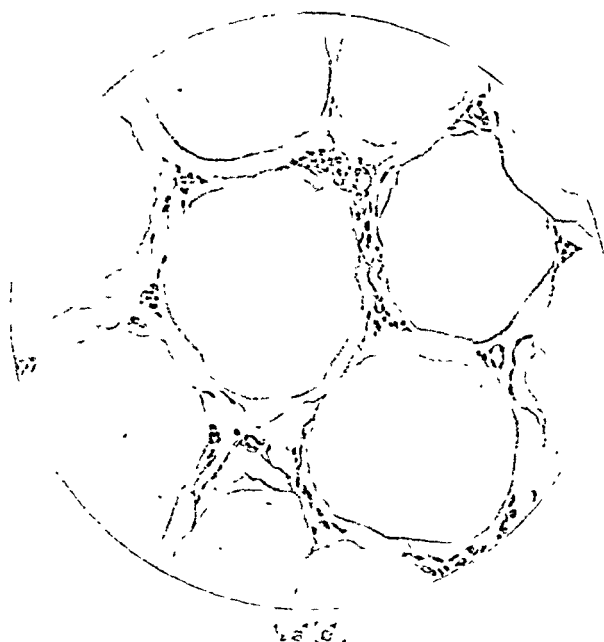


Fig. 2. Section through testicle of a rabbit 6½ months old, semicastrated at an age of 6 weeks. The animal had the penis of a castrate. The intertubular tissue is rich in connective fibres and spindle shaped nuclei. Interstitial cells with a small area of protoplasm and with a smaller nucleus. Seminal tubules in full spermatogenesis (not drawn) and of the same diameter as in Fig. 1. Fixation and stain, as Fig. 1.

were recognizable they had the infantile form, i. e., a smaller nucleus and a small quantity of protoplasm. In general it was difficult to distinguish them from common connective tissue cells. This observation shows that in the presence of spermatogonia and of cells of Sertoli the internal secretion of the testicle is not possible when the interstitial cells are underdeveloped.

An objection can be made against our conclusion: It may be that the animal in the experiment mentioned remained eunuchoid,

not because the interstitial cells were underdeveloped, but because the spermatogenesis had not proceeded far enough. That this objection is not justified is shown by the following observation (6).

B. On two rabbits about six weeks old we performed, for other experimental purposes, unilateral castration; a third animal of the same litter was kept as a control. It is well known that unilaterally castrated animals have fully developed sexual characters. To our great astonishment one of the semi-castrated animals (Prot. No. 95) had at an age of $6\frac{1}{2}$ months the infantile penis characteristic of a castrate; normally the penis of the rabbit assumes its definite adult form at an age of $3\frac{1}{2}$ to 4 months. No mistake as concerns the penis is possible, the differences between an adult and an infantile organ being very striking. But our astonishment became still greater when the animal was killed and the remaining testicle was found to weigh twice as much as the testicle of the control animal; the epididymis was packed with spermatozoa and the microscopical examination showed that the tubules were in full spermatogenesis. There can be no doubt that eunuchoidism is possible in the presence of spermatozoa. The microscopical observation showed further that the interstitial cells were in this case underdeveloped (figs. 1 and 2). Their protoplasm and nucleus were small. In several places cells with a spindle-shaped nucleus, probably connective cells or "quiescent" interstitial cells, prevailed between the tubules. Only a few places with better developed interstitial cells, like those in the two other animals of this experiment, were present. We see that full spermatogenesis with production of spermatozoa, but in absence of fully developed interstitial cells, was in this case insufficient for the performance of the internal secretion of the testicle.

II.

If it is shown that the testicle cannot perform its endocrine function without fully developed interstitial cells, this does not yet mean that the latter are producing the sexual hormones. Two other possibilities are also to be taken into consideration. First, that these cells are necessary for the production of spermatozoa [Kyrle (7), Kohn (1), Stieve (3) and others] which latter would then be the real producers of the sexual hormones. Second, that the interstitial cells serve as intermediaries between the

generative part producing the hormones and the blood into which the hormones have to enter [Berblinger (8)]. But we were able to show experimentally that neither spermatozoa nor any other generative cells, with the possible exception of cells of Sertoli and spermatogonia, are necessary for the internal secretion of the testicle.

A. That spermatozoa are not necessary for the performance of the internal secretion is shown by the following observation (9). On a rabbit (Prot. No. 49) two months old, horizontal incisions in the testicles were made. On the left side the incisions touched probably only the testicle, on the right side also the ductus epididymidis was sectioned. When the control animal which was born the same day, already showed signs of full puberty, the penis of the operated animal was still in an infantile stage. But at an age of about seven months, after we had thought for some time that the animal would remain eunuchoid, a somewhat accelerated development of the penis began and in the eighth month the penis of the animal was almost wholly like to that of the control. The microscopical examination of the left testicle (fig. 3) showed the tubules evidently entered into spermatogenesis. The tubules were lined with several layers of cells which became mostly desquamated, filling the space inside the tubules. The diameter of the tubules was greatly increased as compared with that in an infantile testicle. It is impossible to say whether the spermatogenesis really began in a normal way, because there were in the tubules no cells which could be designated as spermatogonia or spermatocytes. But even if there was a normal beginning of spermatogenesis, this in all cases was stopped by interference of some other factor. The interstitial cells were well developed like in the testis of the normal control animal (fig. 5). Dr. Wagner found even several mitoses, a phenomenon very rare for interstitial cells. The microscopical examination of the right testis gave somewhat similar results.

This observation leaves no doubt that full development of a sexual character which depends upon the internal secretion of the testis, is possible without any spermatozoön having developed. As to the question whether other stages of spermatogenesis are necessary for the entrance of the testicle into puberal hormonal activity, this observation gives no definite information, as it was

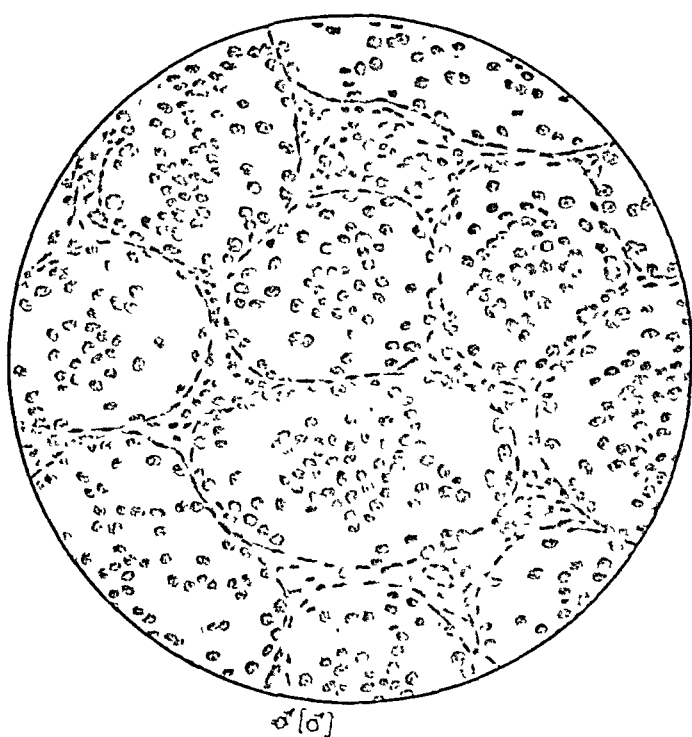


Fig. 3. Section through testicle of a rabbit 8½ months old; horizontal incisions on the testis made at the age of 2 months. Normal penis. Interstitial cells well developed. Seminiferous tubules in a state of degeneration; desquamation of cells which seem more likely to be cells of Sertoli. Fixation, Bouin; stain, Hem-Eos.

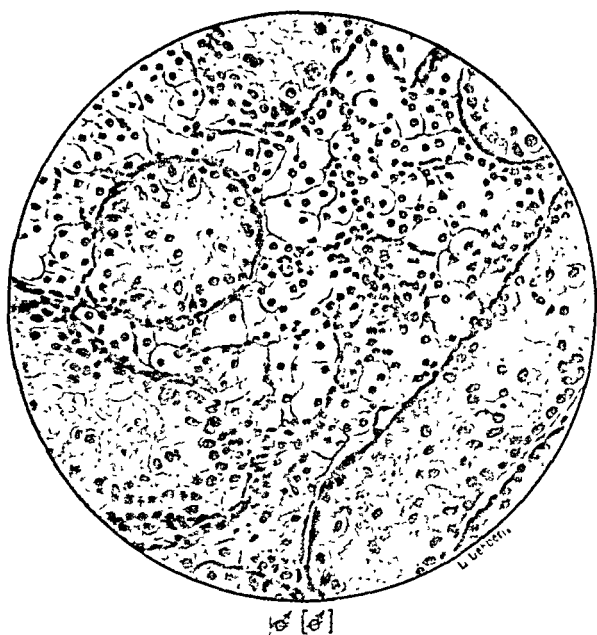


Fig. 4. Section through testicle of a rabbit 8½ months old, horizontal incisions through the testicle and ductus epididymus at the age of 2 months. The animal had the penis of a castrate. Interstitial cells of extraordinary dimensions packed full evidently with fat. Seminal tubules in a state of degeneration; they seem to be less developed than in Fig. 3. Fixation and stain, as Fig. 3.

not possible to make any precise statement as to the character of the desquamated cells.

B. Now I will give an example which shows that full hormonal activity of the testis is possible even in the absence of all stages of spermatogenesis (10). On a guinea pig (Prot. No. 30) about ten days old, partial castration was performed: the left testis was wholly removed and from the right testis only a small fragment from the upper pole was left in the body. When the animal was seen four months after the operation the penis with the intromittent sack and the horny styles was found normally developed. Then the animal was killed. The vesiculæ seminales were found normal in every respect as compared with the normal control animal. The testicular fragment was found embedded in the fat tissue covering the upper pole of the testicle of the guinea pig. The fragment was of a reddish brown color, more or less similar to that of the liver. The vascularization of the fragment was very good. The microscopical examination of this fragment showed that all the tubules without any exception were in a state of degeneration. There was only one layer of cells in the tubules, most likely cells of Sertoli and perhaps—I never could state it with certainty—some spermatogonia. The total volume of this fragment was very exactly calculated to be about 20 cc.

This observation seems to show that full hormonal activity is possible even in absence of all the stages of spermatogenesis, i. e., when the tubules by a “regressive development” are brought to a juvenile stage (11).

Against this conclusion one could make two objections:

(1) It may be that after the seminal tubules had remained in a juvenile stage for a certain time, signs of castration would show. But we have observed an animal treated in the same way, for eleven months, without somatic signs of castration appearing. A temporary regeneration of generative tissue as probably occurring in testicular fragments might indeed have interfered and by this the maintenance of the sex characteristics might be explained. But no proof exists that such a regeneration always takes place. Tiedje (12) assumed that there is, after a degeneration of the tubules has taken place, a pause in the endocrine function of the testicle till regeneration occurs; but this is wholly erroneous, since out of a great many cases I only once observed

temporary cessation of the endocrine function of the fragment with following resumption of endocrine activity.

(2) A second possibility would be that the testicle can, indeed, perform its normal hormonal function without the different stages of spermatogenesis being present, but that spermatogenesis is necessary for the development of the interstitial cells to an organ of internal secretion. If we compare the animal

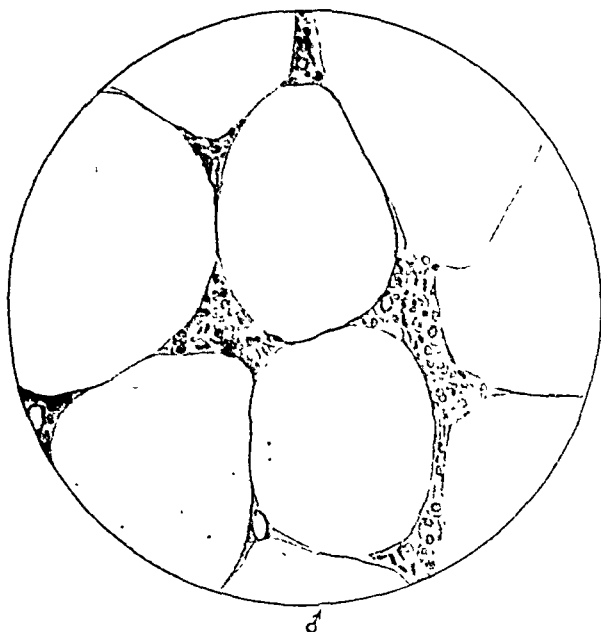


Fig. 5. Section through the testicle of a normal animal of the same litter as Fig. 4. Seminal tubules in full spermatogenesis (not drawn). Normal interstitial cells. Fixation and stain, as Fig. 3.

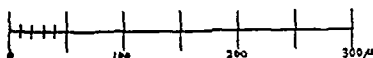


Fig. 6. Scale of magnification.

No. 4 with No. 30 such an assumption becomes very suggestive. In No. 4 we have infantile tubules and infantile interstitial cells with eunuchoidism; in No. 30 we have tubules regressed to an infantile stage and adult interstitial cells with sexual maturity. On taking into consideration only the actual state of the testis one must conclude that the different result is caused by difference in the state of the interstitial cells, but taking into considera-

tion what had happened in the testis of both cases in the course of several months, one cannot exclude the possibility that beginning spermatogenesis, if indeed not a complete cycle, was necessary for the development of active interstitial cells. By such a point of view we analogize between what happens in the testicle and in the ovary, since in the latter it is believed that the transformation of inactive connective cells into active hormonal elements takes place by means of development of generative cells, i. e., by follicular development.

Berblinger (8) is disposed to think that our small testicular fragments were sufficient for a normal masculinization because the interstitial cells were hypertrophied and by this the resorption of the hormones which, according to him, are produced by the generative cells, was intensified. But this suggestion is not justified since small fragments can perform a quantitatively normal hormonal function even when there is no, or very insignificant, hypertrophy of the interstitial cells as we have shown in another paper (13).

III.

Against the theory that the interstitial cells play a rôle in the internal secretion of the testis the objection was made by several authors that there are cases where no signs of testicular hormonal activity have been observed although interstitial cells were present in great quantity. Such cases were reported by Bell (14), Benda (2), Dürck (15), and Berblinger (8). Experimentally such a situation was claimed to have been caused by Stieve (16). It is impossible to give here a detailed criticism of all the separate cases reported; the criticism in Stieve's case should be rather a severe one. I will mention only what we observed personally. On an animal (Prot. No. 41) of the same litter as No. 49 (see above) horizontal sections through the testis and the ductus epididymidis were made on both sides. The animal was observed for about six months. It remained eunuchoid as shown by the observation of the penis. Microscopical examination (fig. 4) of the testicle showed that spermatogenesis had ceased at a somewhat earlier stage than in No. 49; the diameter of the tubules was remarkably smaller than in the latter case; there was mostly only one layer of cells and only rarely desquamation. The interstitial cells were present in great quantity. Their dimensions were extraordinarily great, apparently due to

the fact that the protoplasm was packed full of droplets of fat. No differential stain for fat was employed, but the large vacuoles separated only by very small threads of protoplasm can be, I think, interpreted as remains of droplets of fat. In normal rabbits, guinea pigs and mice I never saw a similar picture. The nuclei of these cells was in general normal, but often they seemed to be pyknotic (?). In some places apparently normal interstitial cells were to be found. Many questions arise here. Were the interstitial cells normal or not and is the eunuchoidism in this case to be explained by an abnormality of the interstitial cells? Or was the eunuchoidism caused by a cessation of spermatogenesis? And if the latter is true what mechanism was here at work? Was the production of hormones impossible because the generative cells as the supposed producers of hormones have not developed? Or did the normal development of other hormone producers, i. e., the interstitial cells, become impossible because of the lack of one of the hypothetical conditions of this development, the lack of spermatogenesis? Were the interstitial cells normal or functional in all the reported cases in man? No answer can actually be given to all these questions. Much further experimental work is needed before we shall be able to decide among all the possibilities mentioned above.

IV.

We have seen that it is almost sure that normally developed interstitial cells are necessary for the normal hormonal action of the testicle, whereas no definite conclusion can be drawn as to the significance of different stages of generative cells for this function. Recently Stieve (3, p. 79) suggested that the hypertrophy of the testicle after unilateral castration is a proof of the endocrine function of the generative part. The increase in weight of the remaining organ is caused by an increase of the seminal tubules, and Stieve argues that this increase is nothing else than a compensatory hypertrophy of the generative part. But in a great number of experiments we were able to convince ourselves that no hypertrophy occurs when only a small testicular fragment is left in the body after the removal of the greater part of both testicles (17). We further were able to show with certainty that such a small fragment can substitute for two normal testicles in their hormonal function (5). In the case No. 30 mentioned above a fragment of less than 1 per cent of the

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testicular mass present in the control animal was sufficient for normal masculinization, as also in some other cases. It follows from this that the hypertrophy of the remaining testicle in unilateral castration is not a compensatory one, i. e., not a hypertrophy caused by an increased endocrine function for the organism as a whole. Evidently some other factor not yet known to us is involved in the increase in weight which the remaining testicle undergoes after unilateral castration, a factor which has nothing to do with the hormonal function of the testis (17a).

Indeed, the objection could be made that these fragments are potentially greater, their actual mass being reduced only by the regression of the tubules. This objection is not justified: first, because the tubules are sometimes largely distended even when only one layer of cells is present; second, because the volume of the fragment is small even when compared with that of two whole testicles in which a regression of all the tubules was caused experimentally. But finally we were able to show that development of normal sexual characters is possible when the actual mass of the small fragment is not very far from its potential mass, the greater part of the tubules being in spermatogenesis. We twice made such an observation. In another paper I have discussed this question more fully. (17b). No doubt, no compensatory hypertrophy of the generative part occurs when diminished experimentally, and the increase of the remaining testicle after unilateral castration has nothing to do with the production of the sexual hormones.

On the other hand, we adduced evidence that also no compensatory hypertrophy of the interstitial cells occurs in small testicular fragments (13). As far as hypertrophy of interstitial cells is present it seems to be caused by some local factors among which a good blood supply plays evidently a great rôle (10).

For these questions the reader may be referred to our previous m^{rs}.

as

V.

ation at I learned from my own observations on the histology of the interstitial cells in the testicle of mammals is that they of the demonstrated without great difficulty by staining with there was and eosin, the protoplasm of the cells being strongly mation. The preparations of Dr. Wagner, to whom I am Their dimensions for his histological work, show that the most

useful method of fixation for demonstrating eosinophilia of the interstitial cells is that of Helly (Müller fluid with 5 per cent formalin). Wagner employed in our experiments also other methods of fixation; those of Bouin and of Flemming, and staining by the Heidenhain and Kull-Altmann methods may be especially mentioned.

It would be of great interest to study the question of the interstitial cells in the testicle of mammals from a comparative point of view. We may state that there are great differences between the guinea pig and the rabbit. In the former characteristic eosinophilic interstitial cells appear a few days after birth, whereas in the latter the cells acquire the characteristic appearance of adult interstitial cells only at an age of about three months; I must omit some details here. Now the puberal development of the sex characteristics (the horny styles of the intromittent sack of the penis) begins in the guinea pig a few days after birth, whereas the rabbit enters into puberal development when about three months old. It is not yet certain whether these comparative statements, which *per se* are above any doubt, can be employed as a proof for the theory of the endocrine function of the interstitial cells. As far as we have seen, the beginning of puberal development of the sex characters is more or less synchronous, not only with that of the interstitial cells, but also of the generative cells. Let us hope that further research work along these comparative lines will be carried out by histologists.

The case of the triton is of especial interest from a comparative standpoint. Bresca (18) has shown by means of castration that the characteristic nuptial feature of the male triton is under the control of the testicle. This was lately confirmed by Aron (19), who showed that by bilateral castration a complete standstill in the development of the nuptial feature is determined when the operation is performed at the beginning of this development. As no interstitial cells are to be found in the intertubular tissue in the testicle of the triton its case was taken as a proof that the hormonal function of the testis in mammals cannot be performed by interstitial cells. Stieve (3) especially insisted on this. Such an assumption is erroneous from the outset, as there is no reason to think that in all the different species of the animal kingdom functions should be performed by similar

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the other endocrine glands have on the sex characters, go through the medium of the sexual gland, the latter being some kind of a junction for all those affecting normal feminization and masculinization. Further, it may be that the virility occurring in cases of hypernephroma in women or occurring sometimes in acromegaly (14), have nothing to do with normal masculinization, in the same way that the biochemical disturbances occurring in new growth are not at all similar to the chemical state under normal circumstances.

SUMMARY

The author presents a review of the experiments performed by himself and his co-workers on the interstitial cells of the mammalian testicle. Various data are adduced which have not been published previously. It is held that a normal condition of hormonal activity of the testicle of mammals is not possible without fully developed interstitial cells. A testicle with spermatozoa but with underdeveloped interstitial cells cannot perform its normal endocrine function. Completion of spermatogenesis is not necessary for the performance of the endocrine function. Normal endocrine function is possible even when no other generative cells than cells of Sertoli and spermatogonia are present in the tubules. The hypertrophy of the remaining testicle in unilateral castration is not compensatory since small testicular fragments do not hypertrophy and, furthermore, the sex characters can be normally developed when a fragment of only about 1 per cent is present in the body. The increase of the generative tissue in the testicle after unilateral castration has nothing to do with the endocrine function of the testicle. It is highly probable that the interstitial cells of the testicle are producers of sexual hormones; it may be that in extrauterine life they receive some impulse from the developing generative cells, like the granulosa and the theca interna of the ovary.

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and narrow; respiratory movements and expansion were normal. The lungs were negative except for some possible impaired resonance and slightly exaggerated breath sounds at the right apex. The heart was normal as to position and size except that the left border was palpated $\frac{3}{4}$ inch to the left of the mid-clavicular line. Sounds were clear except for a faint systolic blowing murmur at the apex. There was no decompensation; the blood pressure was 122-90. The abdomen was flat, and there were no masses or other abnormalities. The glands, joints and genitalia were negative. The reflexes were normal. Urine passed in the office showed 0.2 per cent sugar; 24 hour urine, 1440 cc. on usual diet, showed 0.15 per cent sugar; the acetone was moderate and insignificant thereafter. Sugar appeared in slight traces on the 6th day after treatment. His progress was uneventful. On the 16th day he weighed 172 lbs.; there was normal excretion, no sugar and no acetone. On the 25th day his weight was 167 lbs.; he said he felt weak and nervous; nervous twitching was manifest in both legs and he wondered if he needed thyroid extract which had been prescribed at Rochester, Minnesota, and which helped him before. His urinary output was normal and without sugar or acetone. Largely upon his suggestion, thyroid extract, grain 1 (Burroughs and Wellcome), was prescribed daily on April 6th, the 45th day. His weight was then 173 lbs. On April 30th, he felt much better, ascribing the improvement to thyroid medication; he weighed 176½ lbs. and was on a slightly restricted diet. He was next seen on July 15th, working log booms and eating logger's diet. The urine was normal and he weighed 179 lbs.

He was not seen again until August 27th, when he said he had had tonsillitis and pleurisy two weeks before. The pleurisy had been on the right side. Examination showed no signs of fibrinous or serous pleuritis and he was not heard from until December 30th, 1917, when he wrote that he was not feeling well and that the glands under the jaw had been swollen for two weeks and were painful. There was no polyuria and appetite and general health had been normal since July, though he had had two rather severe headaches. He was not heard from then for about 13 months, when he was seen by another physician, complaining of severe occipital headaches. The urine was negative. There were no noteworthy findings. He was not seen then until September 8th, 1919, when he was met on the street. He was feeling well, but there was notable graying of the hair and the eyebrows had grown heavier. Examination of the urine at this time was completely negative and a chemical examination of the blood was made on the next day, fasting, showing sugar 0.083 per cent (normal), urea 27.5, creatinin 1. He had had no glycosuria for a long time, in spite of eating a liberal diet.

He made the assertion that he was always helped by taking thyroid extract.

He was not heard from again until May 17th, 1920, when he had

been admitted to the hospital because of severe headaches for a few days, and chilly sensations in the evening, lasting one or two hours. Headache had been almost constant. He had fever at the hospital, varying from 99 to 100.2; his pulse was .80, and respiration 22. Examination suggested the possibility of meningitis, although there were a few rales on deep inspiration over the right apex. Three days later he was unable to hold things in his left hand. He was nervous, chilly and slightly disorientated. On the 4th day he seemed rather dazed and had a slight muttering delirium. On the 5th day, very definite delirium was present. On the 6th day he had involuntary urination and died two days later. Lumbar puncture had been done on the 5th day of his stay in the hospital. The fluid was not under increased pressure, was perfectly clear, the cell count was only 3, the Nonne was 2+ and the Wassermann was negative. The Lange test was not made at that time. On the same day, definite signs of fluid were found in the left chest, but the clinical diagnosis was meningitis, probably tubercular. Blood examination on the 3d day showed leukocytes 10,000 and polymorphonuclears 68 per cent. Another fact of importance in the light of the autopsy findings was that the skin on the hands, wrists and the neck down to the collar band was unusually discolored and there were a few darkish colored patches on the buccal mucosa.

AUTOPSY

Autopsy on May 25th by Dr. R. L. Benson, Professor of Pathology, University of Oregon Medical School.

The hair was gray, the eyebrows were black and abundant, the axillary, chest and pubic hair was rather abundant and dark brown in color; the forearms and legs were covered with hair. The face and hands had a peculiar yellowish brown color, though the sclerae were clear. The teeth were present, except the right upper second molar. The left upper canine and the left upper incisor were crowned with gold. The mucosa of the lips and mouth was pale, although there was some brownish mottling of the buccal mucosa. There was a linear scar extending across the base of the neck in front, about 15 cm. in length, which was probably the healed scar of a thyroid operation. The body was well muscled. The chest was symmetrical. The abdomen was flat and symmetrical. There was no evidence of disease or injury in the chest or abdomen. The subcutaneous fat was scanty. The ossification of the ribs was normal. The *left lung* was free from adhesions and well aerated throughout, but contained several calcified nodules. The left chest cavity was full of fluid. The *right lung* was adherent at the apex by fairly dense adhesions which were broken with some difficulty. The apex was mostly consolidated irregularly and on cut sections revealed numerous small irregular tubercles, none of which was calcified to any extent. The remainder of the lung was well aerated and presented no abnormalities except a moderate degree

of hypostasis. Microscopic examination showed the miliary and conglomerate tubercles to be very numerous and the process appeared to be active in sections taken from the apices. Other sections showed inspissated and calcified tubercles. There was also a moderate chronic passive hyperemia. *Abdomen.* The omentum was thin and membranous. The transverse colon was greatly distended with gas and the serous surface was moderately congested. The peritoneal cavity contained 100 cc. of clear amber fluid. Throughout the lesser omentum and posterior to it were many caseous nodules, some partly calcified. The *liver* was of normal size and contour; its surface was smooth and presented no marked changes. The *bladder* was distended with urine. The serous surface contained several yellowish gray nodules and the surface in general was of a purplish blue color. The *pericardial sac* contained about 70 cc. of amber fluid. The *heart* was considerably larger than the owner's fist. The left ventricle was firmly contracted, while the whole right side was large, soft and flabby. The right ventricle formed a part of the heart's apex. The auricle was especially distended. The tricuspid valve admitted two fingers, and was fibrous and thickened. The thickness of the left ventricle was 12-14 mm. The region of the aorta was negative. The thickness of the right ventricle was 5 mm. The *right kidney* weighed 200 gm. and was in general pale and firm at the lower pole, while it was soft and a deeper color over most of the upper pole. There were several miliary grayish nodules in the surface of the lower pole. Microscopic examination showed a number of miliary and conglomerate tubercles with large giant cells in the medullary portion. Chronic passive congestion was present. The parenchyma showed relatively little change. The *left kidney* was, in general, normal in size and shape and similar to the right. The cut surface revealed the presence of several miliary to small caseous, irregular masses of yellowish color involving nearly all of the organ. The *pancreas* was somewhat larger than normal and of a light brownish color. In its head and partially surrounding it was a mass of large tuberculous nodules. The organ in general was of a woody consistency. Microscopic examination showed miliary and caseous tubercles to be numerous in the region of the head of the pancreas. The capsule was greatly thickened and the tuberculous process was seen to have invaded the parenchyma. The trabeculae were greatly increased in thickness and number to the extent that there was a marked atrophy of many lobules of the glandular tissue. The islands of Langerhans appeared for the most part to be atrophic, fragmented, and darkly stained. The *right testicle* was normal, but the epididymis contained a caseous tubercle; the *left testicle* and epididymis were normal. Microscopic examination revealed caseous tuberculosis in the right epididymis. The *prostate* was large. It cut more easily than normal and contained multiple caseous tubercles in all lobes. Large caseous tubercles were present in all the sections examined. There was marked atrophy and fibrosis of the gland

tissue. The *right adrenal* was of normal shape, but of greater dimensions than normal; its thickness was over 1 cm. at the lower and outer edge. It weighed 35 gm. The cut surface revealed a succession of large caseous tubercles 5-7 mm. each in diameter and occupying most of the organ. The left adrenal weighed 40 gm. and was similar to the right. Beginning between the *left adrenal* and the aorta and extending down toward the left posterior aspect of the aorta for several centimeters was a chain of firm nodules, ranging in size from a bean to several centimeters each, yellowish in color and on cut surface appearing comparatively lobulated and light gray and containing caseous tubercles. Microscopically, there were numerous large caseous tubercles. The cords of cells in both the medullae and cortices were fragmented, few in number, and widely separated by the congestion of the capillary blood vessels between them. The *thyroid* was present in two lobes, weighing together 35 gm. They showed scattered caseous tuberculosis. Microscopic sections showed the alveoli to contain the normal amount of colloid; the epithelial cells were for the most part low cuboidal to almost flat. There was considerable hyalin formation in the interstitial tissue. No tubercles were found in the sections examined. The *hypophysis* was slightly enlarged and showed diffuse, semicaseous tuberculosis. *Brain and membranes.* The dura was of normal thickness and appearance. The pia arachnoid was moist and irregularly hyperemic. The convolutions were in general flatter and longer on the left side than on the right. In the soft meninges over various sulci were miliary grayish opacities and one was irregular and 3 mm. in length. The anterior portion of the frontal lobes was unusually soft. There were a few miliary tubercles over the lower surface of the cerebellum. Microscopic examination showed that round cell infiltration was well marked in the pia covering the cerebellum. One of the sections from this region showed a pedunculated miliary tubercle. Other sections showed miliary tuberculosis also. The brain itself showed no noteworthy changes.

The *anatomical diagnosis* was as follows: caseous tuberculosis of both adrenals; caseous tuberculosis of the pancreas; caseous tuberculosis of the thyroid; caseous tuberculosis of the pituitary; caseous tuberculosis of the right epididymis and prostate; a few tubercles in the right kidney; caseous tuberculosis of the peribronchial and aortic lymph nodes; active miliary tuberculosis in the right pulmonary apex and healed calcified tuberculosis in both lungs; slight tuberculous meningitis; hemorrhagic cystitis; left cardiac hypertrophy and right cardiac hypertrophy and dilatation; and miliary tuberculosis of the spleen.

DISCUSSION

Since endocrine function is still far from clear, any attempt to explain clinical phenomena on anatomical foundations is

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hazardous, but the following points stand out: (1) In a man of large frame (suggesting gigantism) and with marked hirsutism, a tuberculous hypophysis was found. (2) Peculiar bronzing of the hands and wrists and the pigmentation of the buccal mucosa suggesting Addison's disease, was associated with caseous tuberculosis of the adrenals. (3) Glycosuria was definitely present over three years before his death when he was under my care; caseous tuberculosis of the pancreas was found at autopsy. (4) A colloid goiter was removed 6 years before his death; caseous tuberculosis of the remaining portions of the thyroid was found at autopsy. (5) There was hydrocele operation 10 years before death; autopsy showed caseous tuberculosis of the right epididymis and prostate.

ENDOCRINE THERAPY IN MENTAL DEFICIENCY

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INTRODUCTION

The fact has been established that disorders of the endocrine glands are fairly common among mental defectives. Observations to this effect are of daily occurrence to those whose experience deals with mental defectiveness. At Letchworth Village a survey has shown that about one-third of the inmate population show undoubted evidence of an endocrine imbalance. Raeder reports that pathological changes in one or more of the ductless glands were discovered in seventy-six out of one hundred cases of feeble-mindedness coming to autopsy. Timme has pointed out a peculiar conformation of the sella turcica in Mongolism, which is possibly related to a pathology of the anterior lobe of the pituitary.

Whether a glandular imbalance is responsible for the stunting of intellectual growth or whether it is only a part of a general tissue inferiority, no one is able to state. Both are probably correct. The matter resolves itself into determining, if possible, what the exact relation may be. There have been cases reported where the mental defect seemed closely dependent on glandular elements, while there are other cases where the endocrine dysfunction seems to be merely one of the various symptoms of a general and widespread inferiority.

Glandular therapy, according to reports on an occasional case, has proved of value in stimulating intellectual development; in other cases it has been a distinct failure. What are the fundamental characteristics which in one type of case warrant hopes of improvement, while in the other indicate that glandular treatment is useless?

Before endocrine therapy can prove of any real practical value in mental deficiency we must establish certain criteria which will aid in the selection of cases, that may be materially benefited by treatment. It is with this idea that glandular treatment has been tried on a few selected cases at Letchworth Village.

The cases chosen belonged to three endocrinopathic groups, namely, the status-thymico-lymphaticus, the hypothyroidal, and the dyspituitary. Most of these cases, although corresponding more or less closely to the group in which they were classed, also showed one or more characteristics of either one or both of the other groups. It is well to realize at the outset that nearly all cases of endocrine disorders among the feeble-minded are of pluriglandular significance.

The cases studied had been in the institution for a year or more. Consequently their habits, reactions, and rate of progress were fairly well established. Immediately before instituting treatment, they were given a thorough physical examination, including height, weight, blood pressure, and blood sugar content. Their intelligence was measured by the Terman scale and a few characteristics such as alertness, industrial efficiency, energy, social adaptability, and mood were noted. Other symptoms referable to the glandular disturbance, such as headache, lassitude, fatigability, enuresis, and menstrual abnormalities, were observed.

These cases were then placed on glandular therapy; ample precautions were taken to insure its being carried out conscientiously, and the observations were repeated six months later.

Any changes in the physical characteristics and build were noted. In determining the influence on the rate of accretion in stature and weight it was essential to express any such increase in relation to the normal rate of growth for the various ages represented by the cases in this study, as many of them were still in the developmental period. Changes in the systolic, diastolic, and pulse pressures were determined. The blood sugar content was again determined at the end of the six months' period of glandular feeding.

The influence of endocrine therapy on the growth of intelligence was determined by comparing the amount of increase during a control period with the amount during the six months' treatment. Although in many instances these tests were not

given by the same individual in the first and second examinations, they were given by observers of adequate experience.

After due consideration it was thought best to disregard any margin of error, first, because if such was not done, matters would be so complicated that nothing could be said concerning the results; and second, if such a margin was given consideration, to be accurate, it would have to be considered as possibly affecting either favorably or unfavorably both the positive and negative cases.

THE STATUS-THYMICO-LYMPHATICUS GROUP

This group consisted of nineteen cases. All except one were males. Their ages ranged from $8\frac{1}{2}$ to $19\frac{1}{2}$ years. The average age was $13\frac{1}{2}$ years.

Physical Characteristics: In general build they were rather slender and loose-jointed. The skin was of a soft, velvety, delicate texture with a noticeable absence of the usual fine hairs. In all cases the genitals were small and under-developed. In three cases the gonads were undescended. Fourteen showed a varying degree of inversive characteristics. Nine were chronic bed-wetters.

Height: Ranged from 123.4 cm. to 158.2 cm. The average was 139.2 cm.

Weight: Ranged from 53 lbs. to 105 lbs., the average being $76\frac{1}{4}$ lbs.

The *index of build*, based on the average height and weight of this group, was 24. The average index of build for normal males at $13\frac{1}{2}$ years is 26.

Blood Pressure: The systolic blood pressure ranged from 75 to 120, with an average of 95. The diastolic pressure ranged from 60 to 80, with an average of 74. The pulse pressure in all the cases was noticeably low, and the average for the group was 21, or about thirty per cent of the diastolic pressure.

The *blood sugar* content, obtained after a fourteen hour fast, was decidedly low in all cases. It ranged from .038 to .090, with an average of .060.

Intelligence: The percentage of normal intelligence ranged from 17 to 76. The average was about 55. This group consisted of one idiot, three imbeciles, eleven morons, and four borderline types.

Personality: With the exception of two subjects who were unusually stubborn and irritable, there was nothing of note in the personalities of these cases.

Treatment: Endocrine therapy was carried on with the patients continuing under the same living conditions. Treatment consisted of Armour's desiccated thyroid and whole gland pituitary substance given by mouth. Minimal doses were used at the start and gradually in-

Intelligence (Table V): In ten cases of the group there was no gain in mental age. In two the gain was of doubtful significance. In seven, however, the gain was quite striking, especially when one considers that a gain of 5 or 6 months in 5 cases, and a gain of 12 and 19 months respectively in two other cases was made in a short period of half a year; it is also to be remembered that the increase stated above is that in excess of the expected gain. Table VI shows the ages of these subjects who improved.

Personality: There were no changes in character or temperament of any case in this group.

TABLE IV—BLOOD SUGAR

	NO. OF CASES		
	Status Group*	Hypothy. Group	Dysplt. Group
Stationary	0	14	17
Decreased to normal.....	0	2	0
Increased by .020 to .029.....	1	0	0
Increased by .030 to .039.....	4	0	0
Increased by .040 to .049.....	1	0	0
Increased by .050 to .059.....	5	0	0
Increased by .060 to .069.....	1	0	0
Increased by .070 to .079.....	3	0	0
Increased by .080 to .089.....	1	0	0
Increased by .090 to .099.....	1	0	0

TABLE V—INTELLIGENCE

(Based on expectancy of gain in Terman test for a six month period as determined by actual gain prior to treatment.)

	NO. OF CASES		
	Status Group	Hypothy. Group	Dysplt. Group
Not exceeding or less than expected gain.....	10	11	14
Exceeding expected gain by 2 to 3 mos.....	2	0	0
Exceeding expected gain by 4 mos.....	0	1	0
Exceeding expected gain by 5 mos.....	3	0	1
Exceeding expected gain by 6 mos.....	2	1	1
Exceeding expected gain by 7 mos.....	0	0	1
Exceeding expected gain by 8 mos.....	0	1	0
Exceeding expected gain by 12 mos.....	1	0	0
Exceeding expected gain by 15 mos.....	0	1	0
Exceeding expected gain by 17 mos.....	0	1	0
Exceeding expected gain by 19 mos.....	1	0	0

SUMMARY

The results of endocrine therapy in the status-thymico-lymphaticus group are as follows. There was no change in general build or texture of skin. In two cases distribution of hair became more normal. In three cases descent of the testes into the scrotum occurred during treatment. Of nine chronic bed-wetters, 7 were relieved of their enuresis. This, however,

* Two cases not estimated. Vein could not be tapped.

may have been a matter of training, as such results are not uncommon in cases receiving no special treatment. In eleven cases the normal rate of growth was definitely exceeded. In ten cases the normal rate of increase in weight was exceeded by one to six pounds. The index of build remained unchanged. In practically each case the vascular tone was substantially improved. In each case the blood sugar content was raised to well within normal limits. In seven cases there was a definite increase in mental age. In five of these there was increase practically month for month for the time under treatment; one showed an increase of two months and one an increase of three months in mental age for each month of the period in which glandular therapy was carried on. There were no character changes in this group of cases.

TABLE VI—ACTUAL AGE OF THE FIFTEEN CASES SHOWING AN INCREASE IN INTELLIGENCE

A. Status-Thymico-Lymphaticus Group

Intelligence gain (in months)	Actual age (in years)
5	8
5	13
5	14
6	9
6	13
12	12
19	16

B. Hypo-thyroid Group

Intelligence gain (in months)	Actual age (in years)
4	14
6	9
8	18
15	13
17	14

C. Dyspituitary Group

Intelligence gain (in months)	Actual age (in years)
5	26
6	16
7	23

HYPOTHYROID GROUP

This group consisted of sixteen cases. Fourteen were females and two were males. Their ages varied from 8 to 19 years. The average age was 12 years, 2 months.

Physical Characteristics: In general build they were all inclined to be short and stocky. The long bones were short, the hands more or less trident in shape, the bridge of the nose flattened, the lips thick, and the skin dry, scaly, and thickened. The hair was noticeably dry and in three cases there was a marked seborrheal eczema of the scalp.

The *height* ranged from 118.0 cm. to 154.3 cm., the average being 131.7 cm.

The *weight* ran from 45 lbs. to 159 lbs., with an average of 75 lbs.

The *index of build*, based on the average height and weight, was about 27.5. The normal index of build for the average of the ages represented in this group would be about 25.

Blood Pressure: The systolic pressure varied from 78 to 150, with an average of 101. The diastolic pressure varied from 60 to 80, with an average of 78. The pulse pressure was rather low, the average for this group being 23 or about 35 per cent of the diastolic pressure.

The *blood sugar* estimation, the sample having been obtained after a fourteen hour fast, showed a content ranging from .077 to .140, with an average of .097.

The *intelligence* quotient ranged from 24 to 75, with an average of 46. In this group were seven imbeciles, eight morons, and one borderline type.

Personality: With but few exceptions the members of this group ere of a dull, lethargic, listless, easily fatigable, phlegmatic type.

Treatment: Glandular treatment was prescribed and carried on under careful supervision. It was found that the subjects could tolerate thyroid substance to the limit of three to six grains daily. Iodine in the form of sodium iodide was given along with the thyroid. Later during the course of treatment whole gland pituitary substance was added and in some cases was run up as high as three grains daily. Three cases, which were originally started in this group had to be discontinued, two developing pulmonary tuberculosis and one developing a hypomanic mental state.

The following observations were made after a six months' course of treatment

Physical Characteristics: The general build remained unchanged. There was a noticeable difference in the texture of the skin in every case. In every instance the skin became smooth, moist, and quite normal in texture. The hair ceased to be dry and brittle, and the three cases of seborrheal eczema entirely cleared up; these cases had heretofore resisted all efforts in the form of inunctions, washes, and other local applications.

Height (Table I): Six subjects either remained stationary, grew at a rate slower than normal or grew at a rate consistent with the normal. Two that did not increase in height were over 16 years of age. Of the two that did not grow as rapidly as normal, one was 8 and one was 12 years old. The two that grew at the same rate as the normal for their respective ages were 8 and 13 years old. Of the ten that grew at a rate exceeding the normal for their respective ages, three were between the ages of 16 and 19.

Weight (Table II): Eight subjects, or just one-half of the number in this group, showed a net gain in weight ranging from two to nine pounds each.

The *index of build* remained essentially unchanged.

Blood Pressure (Table III): In over half of the subjects the blood pressure was not materially affected. The average systolic pressure after treatment was 104, the average diastolic 70, giving a pulse pressure for the average of 34, or just about 50 per cent of the diastolic pressure.

The *blood sugar* content (Table IV) was not materially changed except in two cases. In these, a content of .140 and .138 were decreased to .097 and .093, respectively. The average blood sugar content after treatment was .090.

Intelligence (Table V): In five cases the mental age increased well above what would have been expected in each individual case. The figures shown in Table V represent an increase over and above the expected gain based on the rate observed before instituting treatment. Table VI shows the ages of the subjects that improved.

Personality: In but three cases was there any improvement in the stolid, phlegmatic, dull temperament characteristic of this group. These three cases were among those that also showed an improvement in the intellectual sphere as well. They became rather more alert, active, and rather quicker to learn.

SUMMARY

In all cases the general build remained unchanged. In all, there was a definite improvement in the texture of the skin. In three cases a stubborn eczema of the scalp cleared up entirely with glandular treatment. Ten subjects exceeded the normal rate of increase in stature for their respective ages. Eight made an appreciable increase in weight in excess of what would have been normal for their respective ages. The index of build remained unchanged. There was but little change in the blood pressure with the exception that the diastolic pressure fell, thus making the pulse pressure approximate quite close to the normal. The blood sugar content remained essentially unchanged except in two cases where it was originally rather high it was brought down to well within the limits of normality. In five cases there was a definite increase in mental age above what would have been expected from the progress before treatment. Although it cannot be definitely stated, it would seem as though the organotherapy must have been at least a factor in producing this improvement. In three cases, among those that showed the marked increase in mental age, there were certain character changes.

from a dull, apathetic, indifferent state to one of alertness and a greater activity of interests.

DYSPITUITARY GROUP

This group comprised eighteen cases. One subject had a marked intolerance for both pituitary and thyroid substance, either of which produced a severe cardio-vascular collapse, and for this reason could not be continued on treatment. All cases in this group were of females, their ages ranging from 15 to 32. The average age for this group was about 25 years.

Physical Characteristics: The physical characteristics of this group were somewhat variable. Generally speaking, however, the subjects tended to be rather heavy in general build, with a tendency to over-growth in the long bones, narrow maxillae with crowded irregular teeth, half of them having menstrual disorders in the form of scanty, irregular periods, and many of them complaining of severe headaches. Four subjects, although past the age of maturity, had never menstruated.

The *height* ranged from 144.1 cm. to 166.1 cm., with an average of 154 cm.

The *weights* varied from 103 lbs. to 170½ lbs., with an average of 143 lbs.

The *index of build*, based on the average height and weight of this group, was about 38. The normal index of build for the average age represented by this group is about 31.

Blood Pressure: The pressures did not show any marked deviation from the normal. The systolic pressure varied between 95 and 135 mm., with an average of 110. The diastolic ran from 70 to 90 mm., with an average pulse pressure of 33 mm., which was about 43 per cent of the average diastolic pressure.

The *blood sugar* was quite within normal limits in all cases, showing a rather narrow variation from .81 to .115. The average blood sugar was .100.

Intelligence: The percentage of normal intelligence ranged from 27 to 66. There were three imbeciles and fourteen morons in this group. All of them had supposedly reached their limit of intellectual growth. The average I. Q. was 52.

Personality: Irritability and emotional instability with a tendency to sluggishness was, with two exceptions, common to all the subjects in this group.

Treatment: Of all the subjects under treatment those in this group required by far the most attention. Many of them seemed specially susceptible to pituitary substance so that severe headaches, vertigo, and syncopes were not uncommon. The dosage had to be increased with a great deal of caution, although with a few exceptions

they were finally able to take as high as three grains of pituitary daily. In certain cases in which there seemed to be indications of an underactive thyroid gland thyroid was also given. In cases with menstrual disorders corpus luteum was given in courses of ten days or two weeks each month.

At the end of a six months' course of treatment the following observations were made.

Physical Characteristics: There was no change in the general build. Of the four subjects who had never menstruated, three began to have their periods at regular intervals; one of these began one month after endocrine therapy was instituted, one, two months after, and one, three months after. These three were all 16 years of age. Those who had irregularities of their periods showed no improvement. Severe headaches, frontal in character, which were common to the majority of the cases before treatment, almost entirely disappeared.

Height (Table I): In no case was there any increase in stature.

Weight (Table II): With a few exceptions there were no significant changes in weight. Three or four subjects, who were rather obese, lost eight or ten pounds each.

The index or build remained unchanged.

Blood Pressure (Table III): In but five cases was there any change in blood pressure. These cases, however, were those with a pressure somewhat subnormal and during the course of treatment their pressures were brought up to normal.

Blood Sugar (Table IV): In no case was there any change in the blood sugar content which was marked enough to be of any more significance than merely a normal variation.

Intelligence (Table V): Three subjects in this group, although having presumably reached the limit of their mental development prior to treatment, showed a gain of five, six, and seven months respectively; Table VI shows the ages of these three.

Personality: With but two exception, there was no change in the temperament of the subjects in this group. One of those who became more alert and less irritable also had gained six months in her mental age. The other, who had been quite untrainable before treatment, became able to sweep, polish, and make beds.

SUMMARY

Relative to this group the following can be said regarding the effects of glandular treatment: The general build and conformation remained unchanged. Menstrual irregularities were not improved. Of four subjects who had not yet menstruated, three had their initial periods from one to three months after starting treatment, and continued to menstruate regularly thereafter. It is to be pointed out, however, that these girls were

only 16 years of age, and that the one in whom the catamenia did not appear was 26 years old. As would be expected there was no increase in stature in any case in this group. Three subjects, who were much over-weight, lost eight or ten pounds each. Otherwise there were no changes. Only those subjects who showed a pressure below normal were affected. In these the blood pressure was brought up to normal. There was no essential change in the blood sugar. Three subjects showed a definite increase in their mental age which could not be accounted for by a factor of error or normal variation in the test. In but two cases was the character influenced in any way whatsoever. Of these, one patient had shown an increase of 6 months in mental age and become rather more alert and active. The other changed from a useless, vegetating state to one in which she became useful in the grosser tasks of housekeeping.

SYNOPSIS

This paper comprises a detailed report on the characteristics of certain types of endocrine disorders seen among the feeble-minded with a discussion as to the effects of endocrine therapy. Fifty-two cases, chosen with respect to three types of endocrinopathies, were first studied in detail as to general physical characteristics, height, weight, index of build, blood pressure, blood sugar content, intelligence, and personality. They were then subjected to a conscientiously planned and well supervised course of organotherapy given in accordance with certain indications as shown by the physical and mental make-up. At the end of a six months' course of treatment each case was again studied and observations made relative to the various angles of the case as stated above.

For purposes of brevity and clarity it would seem best to take up each endocrinopathic group by itself.

The Status-Thymico-Lymphaticus Group.—This group consisted of nineteen cases, all except one of which were boys. All were quite typical cases from an endocrine point of view. Speaking in averages their age was $13\frac{1}{2}$ years and they belonged to the middle grade moron group intellectually. Endocrine treatment consisted of thyroid and pituitary substance according to the needs of each individual case. Unfavorable reactions, such as severe headaches, vertigo, nausea, and syncope

were common, as a result of exceeding the tolerance, especially to pituitary substance.

Following treatment, 60 per cent of the cases showed a decided gain in height and weight over what would have been the normal rate for their respective ages. Cases in which the gonads were previously undescended showed them after treatment to be in their normal position. At least 85 per cent showed a definite improvement in their vascular tone. In 100 per cent the blood sugar content was increased far beyond what could be accounted for by a normal variation. The blood sugar content in every case had previously been definitely low.

Relative to mental age, in seven cases, or about 37 per cent, there was an unmistakable increase in the intellectual level as measured by the Terman scale. This gain was of special significance in that under no circumstances would it have been predicted on the basis of what each case had done previous to any treatment. This net increase ranged from five to nineteen months.

The Hypothyroid Group.—This group consisted of sixteen cases, ranging in age from 8 to 19, mentally of the low grade moron level; fourteen were girls and two were boys. All showed the characteristic symptoms referable to a persistent and long continued poverty of thyroid secretion.

Large doses of thyroid substance were well tolerated. They were accompanied by iodide and, later, by small doses of pituitary substance.

Naturally, there was no change in the general physical build, but the thick, dry skin, brittle hair, and in some cases stubborn eczema-like eruptions on the scalp were remarkably benefited. In fact, these conditions became entirely normal. Sixty-three per cent showed a material gain in height and weight over what would have been the normal rate for their respective ages.

In about 40 per cent of the cases in this group the blood pressures were below the limits of the normal. Glandular therapy, in each of these 40 per cent, resulted in augmented pressure. The treatment, however, did not affect the blood pressure when it had been normal at the outset.

What has just been said regarding blood pressure also applies to the blood sugar content in the cases in this group. In only two cases, and in these the blood sugar content was quite

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high, was there any material change; in both of these the sugar content was brought down to well within the limits of normality.

Relative to mental development, five cases showed a definite net increase. The increase above the expected rate of progress was 4, 6, 8, 15, and 17 months, respectively, during the six months they were under treatment. In other words, about a third of all the cases in this group showed a definite and unmistakable gain in mental age.

As to improvement of the dull, lethargic attitude common to nearly all cases in this group, but three showed any improvement.

It should be stated that three cases not included in this final report had to be dropped during the first month of treatment. Two developed pulmonary tuberculosis and one became hypo-manic.

The Dyspituitary Group.—The cases in this group were characterized by a tendency to overgrowth of the long bones, with excess weight, narrow maxillae, crowded teeth, severe headaches, menstrual disorders, and considerable emotional instability.

There were eighteen cases in this group, all females, and all adults, mostly between the ages of 20 and 30, although there were five between 16 and 18 years of age. Mentally, they were of the low or middle grade moron in type.

This group presented the greatest difficulty as to endocrine treatment. Susceptibility to overdoses of pituitary substance was marked and the utmost precision was required to prevent severe headaches, vertigo, and, in some cases, cardio-vascular collapse. In fact, one case not included in this number could not be carried along in the experiment for this reason. In certain cases in which the physical condition seemed to indicate it, thyroid was later added to the treatment.

At the end of a six months' period of treatment it was found that this group showed much fewer effects than either the ⁵¹staphylococcus or the hypothyroid cases.

There was no appreciable change in physical characteristics, blood pressure or blood sugar, and as the subjects had passed the period of growth and accretion, naturally there was no increase in height and no significant change in weight, except a slight increase in three that were much overweight. Of four with a

catamenia. three had their periods established one, two, and three months after beginning treatment. These subjects, however, were 16 years old, so that it would be unsafe to assume that the endocrine treatment was responsible for this. Cases with menstrual irregularities, despite the addition of corpus luteum substance to their treatment, were unaffected. Practically all the subjects who had suffered with frequent severe frontal headache were materially relieved. There was no change produced in their difficult personalities, with the exception of two cases. Both of these subjects, although rather irritable, were of a sluggish, phlegmatic disposition rather than emotionally unstable.

As regards the increase in mental age as shown by the Terman scale, three subjects made a net gain of 5, 6, and 7 months, respectively. In none of these was one warranted to expect an improvement, as all had presumably reached the limit of their mental development.

Now considering the results of this preliminary experiment purely as to the question of its effect on the mental defect of our cases, what do we find?

Out of a total of fifty-two cases, fifteen or nearly 30 per cent showed a definite improvement. This improvement consisted of an increase of from four to nineteen months as determined by the Terman scale over what could have been predicted considering their rate of progress prior to instituting glandular therapy. The aggregate net gain made by these fifteen cases amounts to 126 months or an average of 8.4 months for each patient. On examining the individual records of each of these cases it is found that there is a close correlation between the mental and physical improvement. In fact, in every case but one an improvement in the general physical condition, blood pressure, blood sugar content, or net increase in height and weight was found.

CONCLUSIONS

Inasmuch as this is a report of merely a preliminary experiment it would not be wise to draw any hard and fast conclusions. However, it would seem safe to say that endocrine treatment does produce certain changes for the better in deranged physical conditions in that it tends to adjust abnormally low

olism, that it stimulates growth and accretion in those cases still in the developmental period of life, and that in a certain few cases it may be a factor in speeding up or stimulating the growth of a sluggish or enfeebled intelligence.

To be able to predetermine what cases will respond favorably to endocrine therapy is the important issue. This end can be accomplished only by a tedious and painstaking gathering of data on such of the feeble-minded as do show some indication of responding favorably to glandular treatment. It is essential that cause and effect be not confused.

Let it suffice to say, for those who may be inclined to apply this report too generally, that endocrinology may at some time in the future explain the origin and offer a promise of a certain amount of improvement in only a selected small percentage of our mental defectives. Finally, to regard endocrine therapy as a panacea for mental deficiency would curtail what legitimate use it may subserve.

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EXPERIMENTAL INVESTIGATION OF THE VALUE OF THE VARIOUS COMMERCIAL OVARIAN EXTRACTS*

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Much has been done and written on the therapeutic value of the numerous endocrine preparations, but unfortunately, most of the work is empirical in nature. While it is true that many valuable facts have been acquired in this way, still it seems that

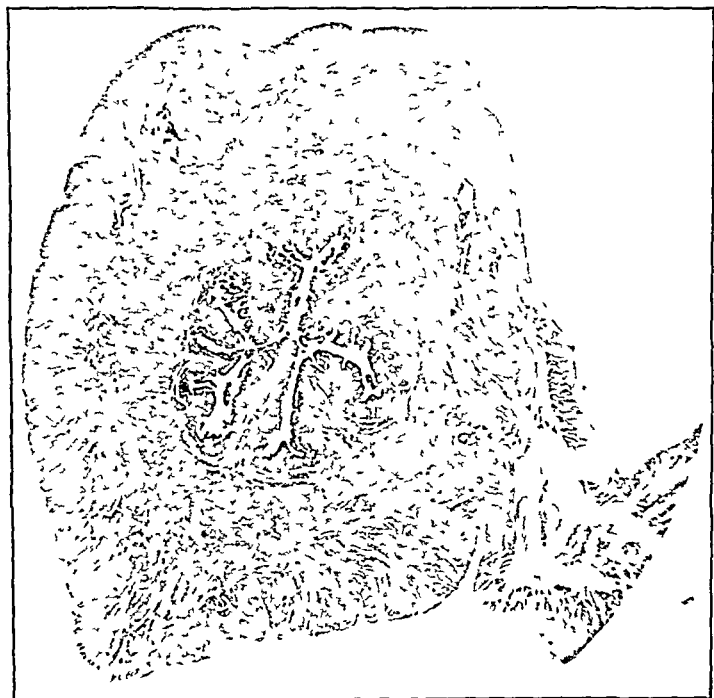


Fig. 1 Uterus 4 days after castration, 3 injections of Parke-Davis Corpus Luteum

the mass of evidence is based on the interpretations of the investigators and the statements of the patients, which statements may be influenced psychically.

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It would be much more advantageous if we could experimentally demonstrate the clinical value or a definite physiological activity of the commercial endocrine products, and be able at any time to duplicate the results.

There are many objections to the empirical method in addition to those mentioned above, for we know that it is extremely difficult at the present time to classify accurately the various types of endocrinological syndromes, with few exceptions, and in addition, the overlapping of groups makes the results of investigation more uncertain.

Certain preparations, we can administer with a fair degree of precision. The thyroid, the adrenal and the posterior pituitary

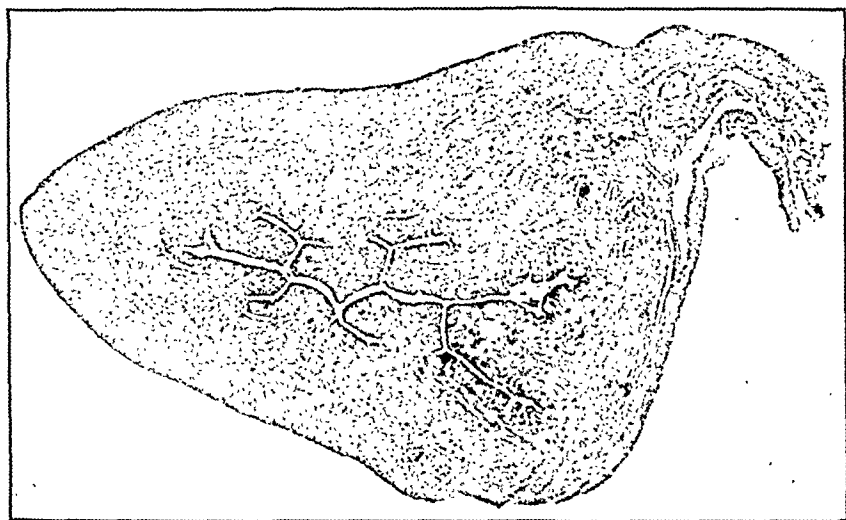


Fig. 2. Uterus 6 days after castration; 4 injections of Hynson, Westcott & Dunning Ovarian Residue.

extracts give a definite physiological response, and experimentally these responses can be shown to be constant.

It was with the intention of establishing some definite method of determining the value of the various ovarian preparations that this investigation was undertaken.

I wish to thank the various manufacturers of these preparations, who so kindly donated the material for the experiments, and expressed their interest in the work and their desire to cooperate, namely, Parke, Davis & Co., Hynson, Westcott & Dunning, The Wilson Laboratories, and Burroughs, Wellcome & Co. Of the Hynson, Westcott & Dunning preparations, we used the

Corpus Luteum, the Ovarian Substance and the Ovarian Residue. Of the Parke-Davis preparations, the Corpus Luteum and the Ovarian Substance with corpus luteum and without corpus luteum was used. Of the Wilson preparations, the Corpus Luteum was used. We did not complete the experiments with the Burroughs-Wellcome preparations, as we found that feeding experiments were too uncertain.

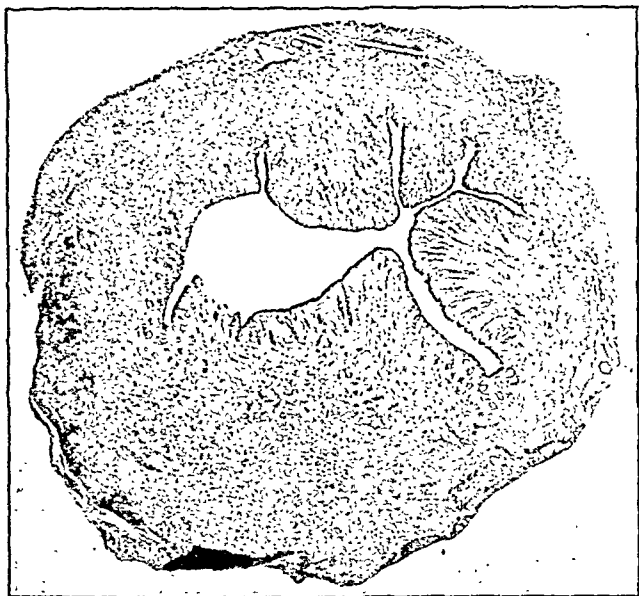


Fig. 3. Uterus 12 days after castration; 4 injections of Wilson Corpus Luteum.

It is a well established fact that after castration a definite atrophy of the uterus takes place, and it was with the idea of using this phenomenon as an indicator that the experiments were undertaken. We attempted to determine, if by the administration of these various preparations by intravenous injections the atrophy could be prevented, minimized, or, if possible, hypertrophy could be obtained. At the same time, the breasts were also observed as well as the thyroid, hypophysis and adrenals, to determine if the administration of these preparations had a definite effect on any of them. Controls were made by subjecting animals to the same operative procedures, but without administering the drugs.

In the beginning we used 1 cc. of the substance for daily injection, but as the animals died after four or five injections, it was decided to increase the time interval between injections, so that 1 cc. was given every third day, beginning from five to seven days after operation.

The castrations were performed in a very simple manner. The animals were anaesthetized, the abdomen shaved and sterilized with iodine. The ovaries and a small portion of the tubes were removed without interfering with the blood supply to the



FIG. 4. Uterus at time of operation.

uterus. At the same time a small segment of the uterus near the horn was removed as a control and one breast also. Before operation the animals were weighed, and when they had recovered from the operation after a period usually of 48 hours, they were put on the same food as before operation.

The fifty-two animals were used. Several died 24 hours after operation of pneumonia and shock. Several died 4-6 days after operation from the effects probably of the daily injections

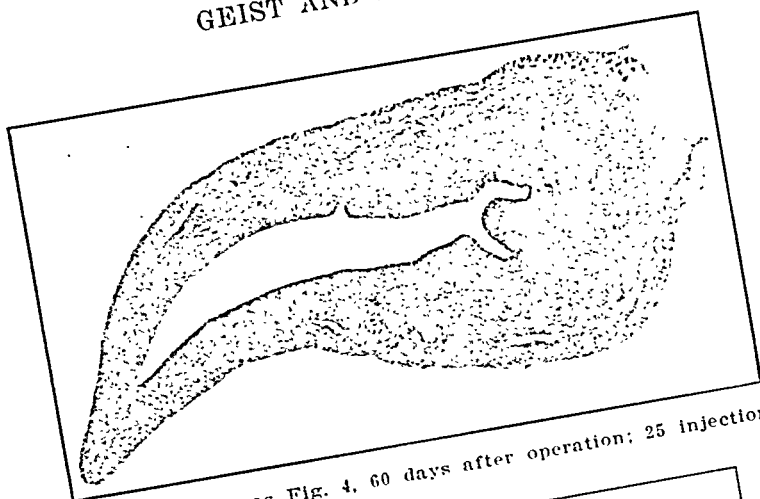


Fig. 5. Same as Fig. 4, 60 days after operation; 25 injections of Parke-Davis Ovarian Residue.

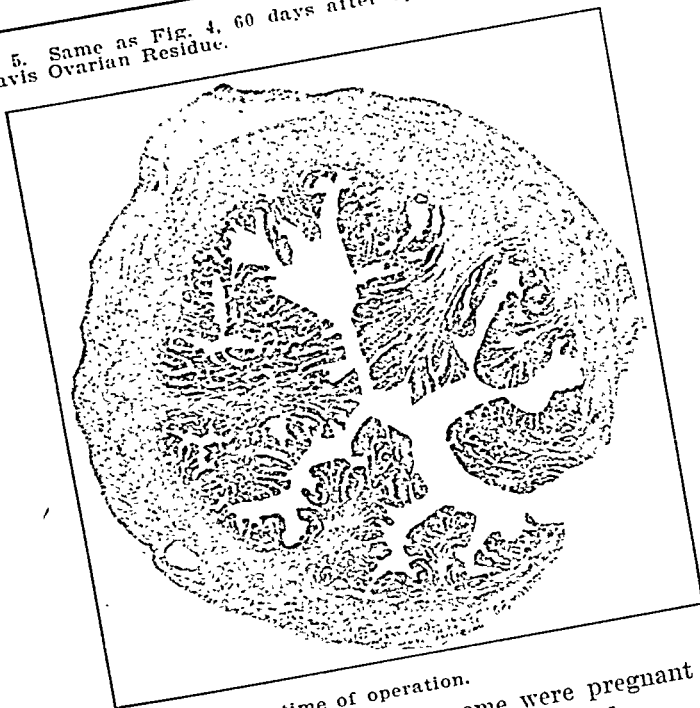


Fig. 6. Uterus at time of operation.

started 24 hours after operation; some were pregnant and unsuited, leaving 38 animals that could be utilized. Of these 38, 5 received Hynson, Westcott & Dunning Corpus Luteum; 4 received Hynson, Westcott & Dunning Ovarian Substance; 5 received Hynson, Westcott & Dunning Ovarian Residue; 5 received Parke, Davis & Co. Corpus Luteum; 5 received

Parke, Davis & Co. Ovarian Substance; 5 received Parke, Davis & Co. Ovarian Residue; 5 received Wilson Laboratories Corpus Luteum. They received from 3 to 32 injections each, extending over a period of from 14 to 85 days after operation. The animals were killed by chloroform and the pelvic organs removed as well as the thyroid, adrenals, pituitary and breast.

In all cases the uterus showed atrophy. In the animals killed early the atrophy was not so marked (Fig 1, 2, 3), as in those that were permitted to live for 2 to 3 months. The atrophy

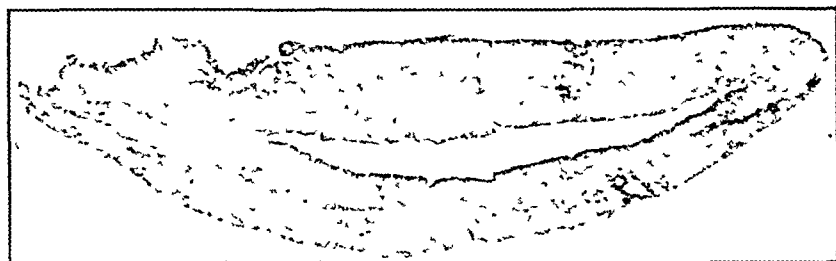


Fig 7 Same as Fig 5 60 days after operation, 25 injections of Hynson Westcott & Dunning Corpus Luteum

involved the mucosa to the greatest extent (Fig. 4, 5, 6, 7). The villi disappear, the stroma, which is represented in most of them as a distinct entity, becomes markedly condensed. The glands disappear and the epithelium of the uterus is represented by one layer of cuboidal epithelium (Fig. 7a). The musculature also shows slight atrophy and a marked loss of tone, the organ changing its shape so that it becomes, instead of cylindrical, a collapsed tube flattened antero-posteriorly (Fig. 5, 7).

One interesting fact noted was that the cervix did not participate in the atrophy (Fig. 8) and it would seem probable that in the rabbit the development of the cervix was not controlled by the ovary. This, too, was true of the control castrates which had received no injections. It is also to be noted that in human subjects, after a supravaginal hysterectomy and bilateral oöphorectomy, the cervix does not undergo atrophy except when the women are near the menopause.

The gross appearance of the pelvic viscera after injection was rather characteristic:—the flattened, rather congested, atrophic uterus was situated in a broad ligament that showed an increased fat deposit.

The breasts, as the uterus, showed marked atrophy (Fig. 9-10). There is an actual diminution in the size of the

organ with a disappearance of the secretory gland tissue and a collapse and diminution in calibre of the ducts. The nipples are markedly shrunk and there is almost complete absence in them of the excretory ducts.

The pituitary gland did not show much change. There seemed to be an increased eosinophilia, but that could not be absolutely determined.

The thyroids of the injected cases appeared somewhat enlarged. In a few there was a tendency to formation of small

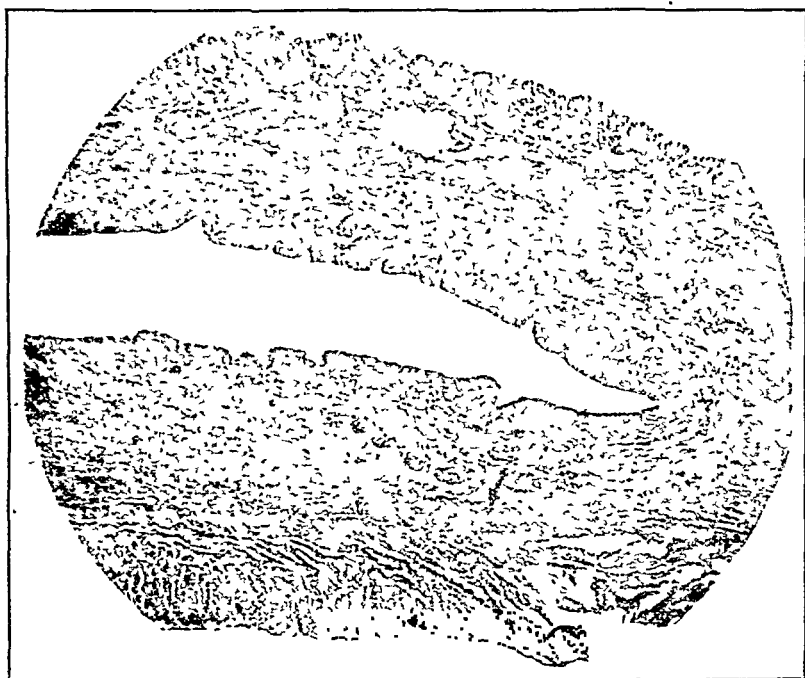


Fig. 7a. High power showing absence of glands, single layer of cuboidal cells lining uterus, condensation of stroma and slight atrophy of muscularis.

cysts. It is possible that this represents a tendency to hyperactivity and may have a bearing on the loss of weight that will be discussed later.

The adrenal showed some interesting changes (Fig. 11). In some there were areas of almost complete necrosis, not large, but scattered throughout the zona fasciculata. In others, definite areas of pale staining cells, containing fat, but very few nuclei.

These, too, were found in the fasciculata and encompassed 6-10 cells. Most of the adrenals show vacuolation and accumulation of fat in the individual cells. Somewhat similar changes were found in the controls, but not so constant nor so extensive.

The weight charts were interesting. The animals used varied in weight from 1.4 kilos to 2.1 kilos at the time of operation and, except for the few instances wherein the earlier stages we gave the injection too rapidly, the animals lost a definite fraction of their body weight. A loss of 0.4 kilograms in the larger

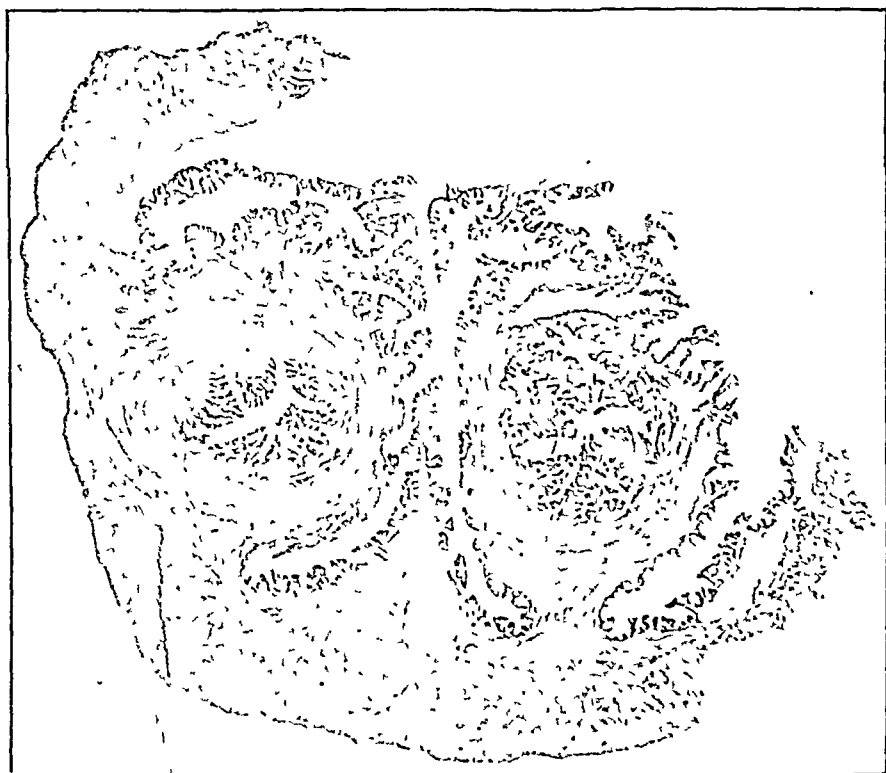


Fig. 8 Cervix showing no atrophy 60 days after castration, 25 injections of Parke-Davis Ovarian Residue

animals was the greatest. The average was 0.3 kilogram or 16 per cent of their body weight. The controls, however, did not lose weight, the gain averaging 0.35 kilos or 11 per cent of the body weight. In other words, there was a decided influence on the maintenance of the weight, probably due to a stimulation of the basal metabolism. We are at present carrying on some experiments in the human female to determine, if possible, the

influence of the ovaries on basal metabolism. To explain this loss of weight we can only suggest that possibly the stimulant to the thyroid, with the resultant cyst formation, is reflected in an increased basal metabolism and this results in the marked loss of weight.

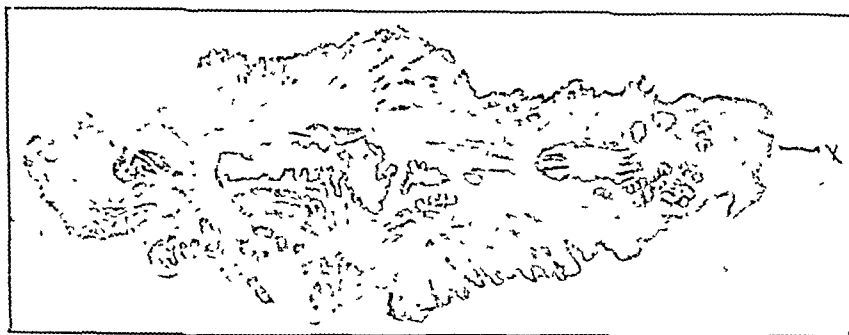


Fig. 9. Breast at time of operation. X marks nipple.

When we analyze our results we find that the injection of the several above-mentioned commercial preparations are unable to prevent the atrophy that follows castration in rabbits. The amounts given are easily the equivalent of the dosage exhibited to human subjects, and we conclude that there is nothing in these preparations, sufficiently active, that will substitute for

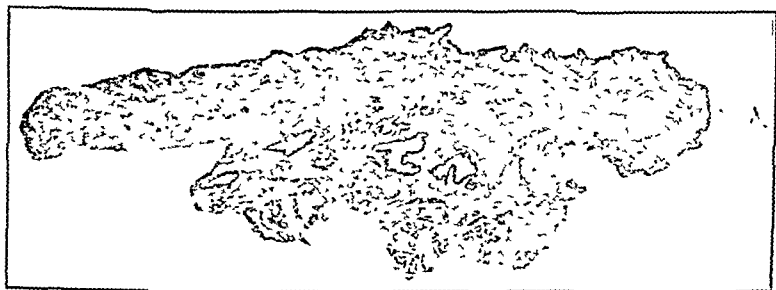


Fig. 10 Same animal as Fig 9, 60 days after castration 25 injections of Parke-Davis Ovarian Residue Breast showing marked atrophy with absence of secreting glands and atrophy of nipple X marks nipple

the hormone that normally maintains the nutrition of the uterus. As these preparations represent all the active epithelial elements of the ovary, we can say that the active substance or substances are not solely situated in the ovary or that they may be destroyed in the preparation.

The cervix does not take part in this atrophy and it would appear more reasonable to suppose, not that the material used was the active factor in maintaining its normal status, but that the castration does not affect it, as can be demonstrated in our controls.

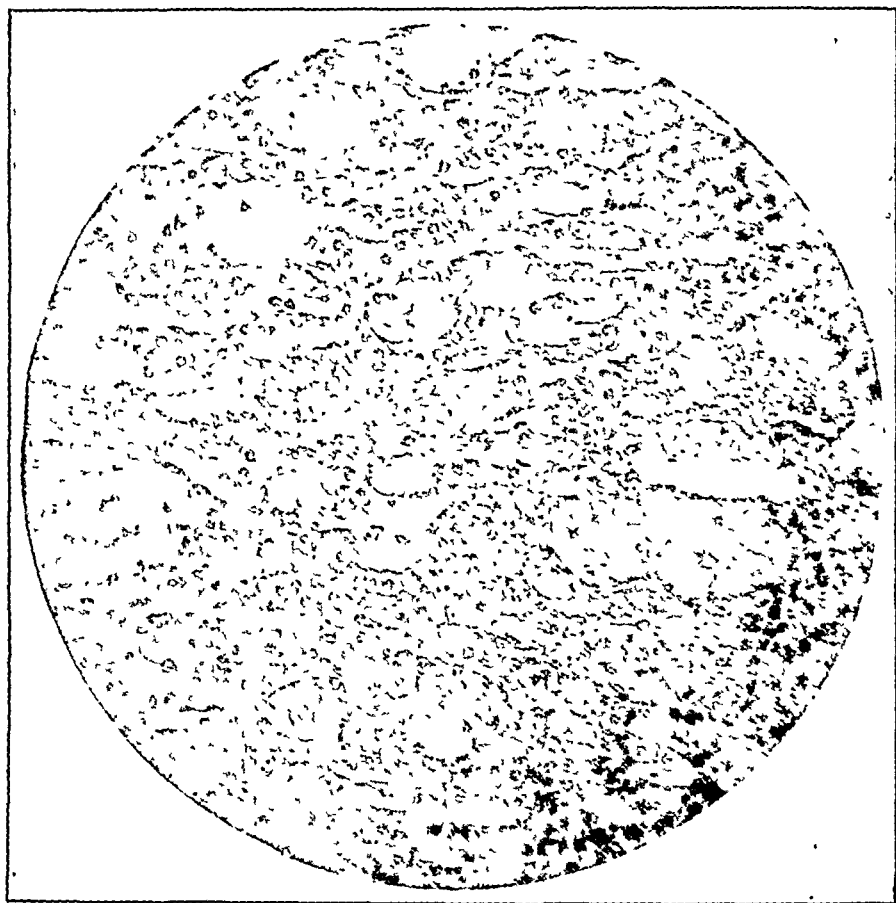


Fig. 11 Adrenal with focal areas of pale granular cells with few nuclei.

The breasts likewise undergo a complete atrophy which cannot be inhibited by the use of these commercial glandular extracts. This same atrophy takes place in the castrates not injected.

Finally, there are some slight histological changes in other glands of internal secretion the significance of which we cannot explain.

The weight constantly decreases, due, possibly, to the action of the preparations. No specific preparation showed itself more active than the others, in this regard.

From these experiments one can conclude that in rabbits the commercial preparations when given in fairly large dosage have no affect in preventing the castration atrophy of the uterus or breasts, but they do cause a definite decrease in the body weight.

We wish to thank Dr. J. Globus for his kindness in preparing the photo-micrographs.

A ROENTGENOGRAPHIC STUDY OF THE SELLA TURCICA IN NORMAL CHILDREN.*

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During the course of a roentgenographic investigation of the sella turcica in children of abnormal mentality, such as found in Mongolian idiocy, myxedema, etc., we soon discovered that a correct interpretation of the x-ray picture was impossible because of our lack of knowledge of what constituted the normal. In turning to the literature on the subject for aid, we were disappointed to find that very little information could be obtained, as the references were meager, consisting of Schuller's investigations some years ago and the more recent work of Jewett; the latter, however, being confined to a study of the normal appearance in the adult. There was nothing that could be found on the sella turcica of the normal child. Timme has published some observations on the appearance of the sella in abnormal children, but has not offered any sellas from normal children as a control.

This lack of literature on the subject in normal children prompted us to discontinue temporarily our investigations in abnormal children and to turn our attention to an attempt to determine, if possible, the size, shape and appearance of the sella turcica in normal children between the ages of 1 and 12 years and, in addition, to note the existence of any possible relationship between the size and shape of the sella and the size and shape of the head. The present study is based upon the x-ray examination of the heads of 104 normal children, ranging between 1 and 12 years of age.

From a roentgenographic viewpoint, the changes in different sellas are those of general shape, changes in the development and shape of the posterior clinoid processes, dorsum sellae and

* A complete description of this study will be found in N. York State J. M. (N. Y.), 1922, 22, 54-58.

anterior clinoid processes. The middle clinoid processes are nearly constant in their shape and development.

The technic used in a study of this kind is important, not so much the exact method used, but the constancy with which it is followed. In adults, teleroentgenography (films taken with the tube at 6 to 8 feet distance so as to obtain nearly parallel rays), is of course the most exact method. In children, however, the long exposures necessary in this technic are not practical. We have therefore selected a tube film distance of 26 inches and, by using a high penetration and milliamperage, have been able to obtain films with one-eighth second exposure. The tube carrier is so adjusted that the central ray passes along a line tangent to the cornea of both eyes and is then moved backward until the central ray passes through the head at a point about one-third of the distance from the external auditory meatus to the glabella. In most instances, this technic gives a good projection of the sella. One can readily imagine that in some rather badly trained children the following of any technic would be difficult even where only an eighth of a second immobility is required. Duplitzed films and screens were used.

It was obvious even from a cursory examination of the films that there was no set normal for the general shape of the sella or for the appearance of the posterior clinoid processes and the dorsum sellae. For purposes of description many different classifications and groupings were tried, some based upon the anterior clinoid changes, some on the posterior clinoid changes and some on general shape. A classification following Jewett's 9 groups in adults was also attempted. None of these groupings and classifications was found feasible because only 50 to 60 per cent of the sellas could be definitely grouped, the rest being border line cases with some characteristics of one group and some of another. In other words, there were many sellas which could not be definitely grouped and would then have been placed in a miscellaneous class which would contain from 30 to 40 per cent of the cases, according to the strictness with which the groups were selected and would therefore be of no descriptive value.

We therefore have decided to classify our cases in 3 very general groups, depending upon the general shape of the sella turcica. In group A are placed those having a generally circularly shaped sella; in group B, those which are ovally shaped,

and in group C, those which are flattened or saucer shaped. Even with this very broad classification, it was not easy to place some of the cases between A and B groups. The rule was followed of placing in B all of those which were not definitely circular in shape.

In group A, the sella has a definitely circular shape, showing always a well developed curved or straight dorsum sellae and posterior clinoids. The anterior clinoids may or may not be developed, but usually are. The dorsum sellae varies markedly in weight and height and also in its shape. It may be very heavy and moderately short or very thin and high or may present a general conical appearance heavier at its base than at its tip. It may be of approximately the same weight at its base and tip. or it may show a bulbous tip which is heavier than the base. The anterior clinoid processes also show rather marked variations. In some instances, they are short, heavy and rounded, in others short, heavy and pointed; in still others, lighter in weight and longer. Occasionally one sees very heavy anterior clinoids which are also very long. In some instances the anterior clinoids are raised above the level of the middle clinoids and are very long. In these latter cases, a slit is seen running anteriorly from above the middle clinoid processes under the anterior clinoids. This slit is in no way a part of the sella. Where the anterior clinoids are rather prominent, the posterior processes may curve forward so as to give the appearance of bridging. This apparent bridging or close approximation of the clinoid processes occurs in about equal proportion in groups A and B. The floor of the sella in group A is necessarily circular in shape.

In group B, the floor of the sella is of oval shape. The posterior clinoid processes and dorsum sellae are always well developed and always curved. The anterior clinoids are almost always well developed and the middle processes usually definite. Both the anterior and posterior clinoids and the dorsum sellae are subject to the same variation as in group A except that the dorsum sellae is never straight.

In group C are placed those cases showing very shallow sellas, those which are very long in relation to their height. In this group also the dorsum sellae is poorly developed or absent and the posterior processes seem to be a part of the superior surface of the body of the sphenoid. The anterior processes may

be well developed, but usually are not. As in group A, in some instances, a slit may be seen running anteriorly from above the middle processes under the anterior; this slit is extra-sellar.

The measurements of the sella were obtained as follows: the length, from the middle clinoid process to the furthest part of the sella posterior; the height, on a line joining the tips of the anterior and posterior clinoid processes, a perpendicular was drawn to the deepest portion of the sella.

A study of the measurements shows a marked variation in the sella of each age. In the first year, varying from 6 by 5 to 9 by 7 mm. Another instance of variation is seen in the two larger measurements, 10 by 8, which occur in the sellas of 4 and 5 years. The smallest sella measured was in a girl of 9 years. The measurements of the sella practically always show a greater length than height, the average ranging from 7 mm. in length and 5.7 in height at one year to 9.2 mm. by 7.1 mm. at 11 years. We were surprised to find that the average length and average height were greater in the sella turcica of girls than in those of boys. We do not know if this is of any clinical significance.

There seems to be a rather rapid increase in size for the first two years and then a gradual increase up to 12 years with, however, much irregularity. The height measurements followed closely those of the length in average, except that they are proportionally smaller.

An analysis of groups A, B and C shows that all but two of group C cases fall in the first 3 years. This seems undoubtedly to be due to the fact that in some instances the dorsum sellae does not ossify early and, as it is not a bony structure at that time, does not appear to be present. Regarding the incidence of groups A and B, there seems to be no definite rule followed except that group A predominates at all ages except at 12 years.

An analysis of the three groups in relation to sex shows no influence of sex on the formation or appearance of the sella, for of group A there were 35 among males and 34 among females; of group B there were 11 among males and 13 among females; of group C there were 6 among males and 4 among females.

Head measurements were made of 50 cases. A careful survey of these and of the corresponding sella measurements seems to show definitely that there is no relation between the size of the head and the size of the sella. The head measurements were

designated and obtained as follows: anterior-posterior, from the glabella to the external occipital protuberance; anterior-posterior maximum, over the greatest length of the head; lateral, the distance between the squamous portion of the temporal bone just above and in front of the pinna; lateral maximum, the greatest bi-parietal measurements. All measurements were made with calipers.

An analysis of the relationship between the size of the head and the sella from the viewpoint of group, demonstrates that all of the group C's occur in small heads. But a small head does not necessarily contain a group C sella, for group C sellas were found in only 50 per cent of the heads measuring less than 17 cm. in length and 14 cm. in width.

CONCLUSIONS

Shape of the sella turcica. The sella turcica in normal children can be classified in a general way by means of the roentgenogram into 3 groups according to shape: A, circular; B, oval; and C, flat and saucer shaped, with modifications as explained in the text. Groups A and B were found in all ages, while group C was practically limited to the first 3 years.

Shape of sella as to size of the head. The shape of the sella has no significance except in the case of the flat group C type. This type is always found in small heads, but it does not necessarily follow that all small heads exhibit this type.

Size of sella in comparison with age of the child. There is a marked variation for each age, both as to height and length of the sella for that particular age. The average height and length of the sella shows a comparatively rapid increase in the first 2 years with a gradual yet irregular increase from then on up to the age of 12. There is a tendency for the average height always to follow the average length increase.

Both the sella as to size of head. There is apparently no correlation between the size of the head and the size of the dorsum sellae in all measurements.

In group C sella as to sex. There is no difference between the three groups between the heads of boys and girls. This group also does not seem to be any influence of sex on the posterior preformation of the sella. The sella of girls, surface of the body of sella both length and height.

RELATION OF ONSET OF MENSTRUATION TO ENVIRONMENT

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It is generally conceded that girls in small towns and hamlets begin to menstruate later in life than girls in larger towns and cities. De Lee, in his text book on obstetrics, states, "The highly strung city girl has her periods early in life, the country girl, later. The poor overworked factory girl later—the rich girl early."

Hirsh, in his text book on obstetrics, states, "The environment of a girl determines the age at which menstruation begins. If she lives in a city, subjected to indiscriminate association with those of the opposite sex and the sexual temptation, the function appears earlier than in the country."

Osborne states, "Early menstruation has at present become more frequent because this is an age of excitement and nerve tension even for girls—anything that increases thyroid activity in young girls will hasten puberty and the thyroid activity is increased by sexual excitement."

These various views mirror the general opinion of the medical profession of the present day as to the onset of menstruation.

We have made a careful analysis of the menstrual histories of 800 consecutive women as they presented themselves in our (W. Lintz) private office practice. These represent the various social, economic and racial strata which compose our present society. Our findings show that the environment has less to do with the onset of menstruation than is generally supposed. It

seems to us that heredity plays a very important rôle which is tantamount to saying that the incertory organs are the underlying factors in the determination of puberty.

Girls of similar endocrine characteristics in a given family have a similar menstrual onset. In such a family all the girls need not necessarily begin to menstruate at a given age, because they happen to be in the same environment, but all those of similar endocrine heritage will do so, whereas those of dissimilar endocrine heritage will not, irrespective of environment. Several girls of a large family will begin to menstruate at the age of 13 or 14 years in a small town or on a farm—while the other sisters, brought to a large city such as New York, working in factories and stores, will begin to menstruate at the same age. In still other cases, one girl will begin to menstruate at 13 to 14 years on a small farm while another sister will begin at 17 or 18 years on the same farm. We have city girls beginning at 17 or 18 years and country girls at the age of 11 or 12 years. Relation of onset of menstruation between mother and daughter will depend upon their endocrinologic heritage rather than on any other factor.

We have attempted to tabulate our findings according to the age of onset of menstruation and according to the size of the community in which the subjects resided at that time. The first column includes scattered farms, hamlets, villages and towns up to about 3,000 to 4,000 population. The second column includes towns of 5,000 to 25,000. The third column includes cities of 50,000 or over.

ANALYSIS OF 800 CONSECUTIVE CASES

Age Onset of Men- struation.	Farms, Hamlets & Towns up to 4,000		Towns 5,000 to 25,000		Cities 50,000 and over	
	Percentage.	No. Cases.	Percentage.	No. Cases.	Percentage.	No. Cases.
12	1 $\frac{5}{8}$ %	13	2 $\frac{1}{2}$ %	20	3 $\frac{1}{4}$ %	26
12 to 14	35 $\frac{5}{8}$ %	285	6 %	48	21 $\frac{7}{8}$ %	175
15	5 %	40	3 $\frac{1}{8}$ %	25	5 $\frac{1}{8}$ %	41
16	2 $\frac{3}{4}$ %	22	$\frac{7}{8}$ %	7	5 $\frac{3}{4}$ %	46
17	1 $\frac{7}{8}$ %	15	$\frac{3}{8}$ %	3	1 $\frac{1}{4}$ %	10
18 or over	1 $\frac{1}{2}$ %	12	$\frac{1}{4}$ %	2	1 $\frac{1}{4}$ %	10
Average age of onset of menstruation			Average age of onset of menstruation,		Average age of onset of menstruation,	
13 $\frac{1}{2}$ years			13 $\frac{1}{2}$ years		14 years	

DISCUSSION

Our figures show that 62 per cent of 800 subjects began to menstruate at from 12 to 14 years of age; 35 per cent from 15 to 18 years of age, and 3 per cent after 18 years of age; of these,

two began at the age of 19 and one at 22 years of age. On the farms and in very small towns, the average age of onset of menstruation was approximately $13\frac{1}{2}$ years. In the medium sized towns the average was $13\frac{1}{2}$ years. In the large cities the average was 14 years. Contrary to the existing ideas, this fact shows that environment has nothing to do with the age of onset of menstruation.

It is also interesting to note that in Dr. D. F. Carjel's (1) analysis of 489 women representing many different casts and races in India, the average age of onset of menstruation was 13.63 years. This figure well corresponds with our figures quoted above, although the environment and climate of India is certainly different than in our own group of cases.

Certain specific cases quoted below are interesting examples which illustrate our point, that environment has little or nothing to do with the onset of menstruation.

Case 1: M. L., who lived in a Russian town of 5,000, began to menstruate at 17 years. She has four daughters. She moved to Brooklyn. Three of her daughters began to menstruate at the age of 12 and 13 years and one at the age of 17 years. This case shows that while the mother began late in a small town, one daughter began at the same age and three others at an earlier age in a large city. The determining factor of the onset of menstruation seems to be rather the heritage of similar incretory glands.

Case 2: The mother began menstruation at 14 years in a small Russian town of less than 2,000, while three daughters began in the large city of Brooklyn at a similar age of 13 years, 14 years and 14 years respectively. Hence this case, at least, shows there is no relationship between environment and menstrual onset.

Case 3: The mother began to menstruate at the age of 13 years in a Russian town of 500—contrary to previous ideas of late menstrual onset in small hamlets. She had two daughters who began at the age of 13 years in Brooklyn.

Case 4: M. P. began to menstruate at the age of 16 in Russian town of 10,000. Five daughters began to menstruate in Brooklyn at the age of 15 and 16 years. According to the present view they should have begun to menstruate in a city at a much earlier age. The mother weighs well over 300 pounds, the superfluous weight being possibly of endocrine origin.

Case 5: M. R. began to menstruate at the age of 17 years in Brooklyn. She had four daughters who began to menstruate in New York City at the age of 12 and 13 years.

Case 6: E. S. began to menstruate on a farm at 18 years of age.

Two daughters began to menstruate at the ages of 15 and 13 years respectively on the same farm.

Case 7: M. T. began to menstruate in a moderate sized city of Germany at the age of 18 years. One daughter began in Brooklyn at the age of 18.

Case 8: T. T. began to menstruate at 16 years in a town of 1,000. One daughter began at 12 years in New York City, and three daughters began at 16 and 17 years respectively in New York City.

CONCLUSIONS

These examples are merely taken from a long list of similar cases. They are consecutive cases and represent the poor girl as well as the rich girl, the farm girl as well as the city girl, the school girl as well as the factory girl, the idle girl as well as the working girl, the secluded girl as well as the society girl: all are white girls, but of various nationalities and races. A careful search in all these cases failed to reveal that environment had the slightest influence in determining the onset of menstruation.

Our data shows that regardless of the size of the town or city and of the environment, the average age of menstruation remains approximately the same—13½ years.

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REGENERATION AND TRANSPLANTATION OF THE THYROID

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The following study has been compiled from notes and material left by the late E. R. Hoskins. Most of the material used is from experiments made by him in the spring of 1919, at the University of Pittsburgh, but a few specimens from our earlier work on tadpoles have been used also. The experiments consist of two types of transplantation of the thyroid, and have been grouped together in the hope that they may throw some light on the relation of this gland to metamorphosis.

Some questions were raised by our earlier paper on thyroidectomy (1919), which we could not answer at that time. One was as to the effect of hyperplasia of the gland following incomplete extirpation. One of the tadpoles from that series of experiments metamorphosed at an early date, when it was only about half the size of a normal tadpole at its period of metamorphosis. On examination this animal was found to have a regenerated thyroid which was, in proportion to the size of the animal, several times as large as the normal gland. We supposed that the precocious metamorphosis of this frog was due to its having so great an amount of thyroid tissue, but none of our subsequent experiments have produced a similar result. However, the first two sets of experiments to be described in this paper show some relation between the amount and character of the thyroid tissue and the rate of development.

Another set of experiments was planned with a view to determining whether the thyroid influences directly other phases of metamorphosis besides the skeletal changes involved. In earlier work on this subject we suggested that the metamorphosis of the thyroidless tadpoles was prevented primarily by interference with the calcium metabolism. The transformation to the adult form is a series of steps of which skeletal development is the first, and if the first step be prevented, the later ones may not take place. It is possible that the atrophy of the tail and

other changes involved in metamorphosis would take place in the absence of the thyroid if the skeletal development were normal.

MATERIAL AND METHODS

The animals used in these, as in former experiments were the larvae of *Rana sylvatica*. The operations were performed when the larvae were about 6.5 mm. long, before the thyroid had begun to function. The technique does not need any special description, as it was the same as that previously used and described. Specimens were preserved, usually in Bouin's fluid, and sectioned and stained in the ordinary way.

I. *Regeneration of the thyroid.* Although we have made many attempts to repeat the procedure of 1917 which led to the hyperplasia of the regenerating thyroid and the precocious metamorphosis of the frog, we have never succeeded in obtaining that result again. Cutting the anlage of the gland to bits and leaving the fragments in the animal does not lead to hyperplasia of the organ nor to precocious metamorphosis. A study of the regenerated tissue shows, however, that there is in some cases a hypertrophy of the thyroid which may be correlated with the rate of development of the animal. This condition of the gland and its relation to metamorphosis are illustrated in figures 1 to 5, and 11 to 19. Figures 1 to 5 represent animals in which the thyroid has regenerated, and it will be seen that they are in different stages of development, although all but the last two were fixed at about the same time. The first (fig. 1) is a larva which has grown beyond the size of a normal tadpole at its maximum (cf. fig. 6), but has also developed beyond the condition reached by a thyroidless tadpole (cf. fig. 7). Had it been entirely thyroidless, it would not show so much development of the hind legs as it does. This larva was fixed on the 15th of June, when all the other animals of the series had completed their metamorphosis. Figures 2 and 3 show tadpoles with regenerated thyroids in which metamorphosis is well started. They have developed at the normal rate, and show no peculiarities unless examined microscopically. In figure 4 is shown a specimen which is about to undergo metamorphosis slightly in advance of the controls. It is, however, normal in size and appearance, and is only about two weeks ahead of the controls (fixed in this condition on May 10th). The last frog of this group is the pre-

cocious frog of the 1917 series, reproduced here to scale with the other drawings. This animal, as has been said, underwent metamorphosis a full month before the controls, at a time when it was but half the size of the normal tadpole at maximum.

Examination of the regenerated thyroids of these animals shows that two factors are important in the influence of the glands on the rate of development. One is the amount of the regenerated tissue, and the other is the character of its elements. Certain of these glands show a striking hypertrophy and where this is present a very small amount of the tissue is sufficient to make the animal develop at a normal rate or even a little faster than is normal. This hypertrophy is illustrated (figs. 11 and 12) in the thyroid from the frog shown in figure 4, which has begun metamorphosis a little ahead of the control animals. The follicles of this thyroid are abnormal in size and shape, so that even under the low power of the microscope their abnormality is apparent (fig. 11). The follicles of a normal thyroid (fig. 13) are round or oval in shape and do not have irregular folded walls like those seen in the regenerated gland. A closer examination of the latter shows that the epithelium is not of the normal type. Epithelia from normal thyroids are illustrated in figures 14 and 15, which represent the extremes of variation under normal conditions from a low, flattened cuboidal epithelium with indistinct cell-walls to a high cuboidal with lighter cytoplasm and clear cell-walls. One does not find in normal specimens any such epithelium as is illustrated in figure 12 (an enlargement of part of figure 11) where the cells are of the columnar type.

This hypertrophy of the thyroid is found in those animals which are developing at a normal rate with a very small mass of thyroid tissue, the activity of the cells compensating for their small number. Besides the animal from which the drawings were made, the one shown in figure 2 has a thyroid of the same kind. It has the same kind of epithelium lining the irregular follicles, and is very small. Specimens of the same sort were found in our earlier experiments also.

Not all of the animals in which regeneration of the thyroid has taken place show this hypertrophy of the gland, however, and where it is lacking the amount of the tissue is important in determining the rate of development. This is illustrated in the

three specimens shown in figures 1, 2 and 5, which had varying amounts of normal thyroid tissue. The first has a small amount of thyroid the character of which is shown in figures 16 and 17. The epithelium is flat, but not lower than that found in some normal thyroids (fig. 15). The follicles are of the normal size and shape, but few in number. The figure represents the largest transverse section of the gland, of which but one was present. The thyroid of the animal represented in figure 2 is normal in appearance. That of the precocious frog shown in figure 5 has already been described (Hoskins and Hoskins, 1919), but may be reviewed here. The epithelium is normal (fig. 18), but the amount of the tissue is abnormally great when the size of the frog is taken into account. Figure 19 shows a sagittal section through one of these large glands, of which both have regenerated. The cells lining the follicles are large and appear to be secreting actively, but they are hardly outside the limits of normal variation, and it is evident that if the precocious metamorphosis of the animal was due to the thyroid at all, it is caused by hyperplasia rather than by hypertrophy of the organ.

II. *Transplantation.* In the second series of experiments thyroid anlagen were transplanted from one tadpole to another, with the expectation that these animals with a large amount of the tissue would show the same precocity as the frog with the hypertrophied gland. Although the expected effect was not produced, the results of the experiments called our attention to an interesting point regarding the relation of the thyroid to skeletal development. The animals in question did not reach the stage of metamorphosis earlier than the controls, and it was only on examination of preserved material that any abnormality was observed in them. A number of animals were fixed at the stage just preceding the shrinkage which takes place during metamorphosis, and these were found to have a peculiar shape, as is shown in figure 8. The swollen abdomen suggested at first some abnormality of the viscera, but dissection showed these to be normal. Further examination showed that the development of the skeleton is responsible for the unusual appearance of the animals. The skeleton of the head has developed toward the adult condition faster than the viscera, with the result that the latter are forced out of the narrowed anterior part of the body. This is seen even more clearly in the side view (fig. 9),

and the ventral view (fig. 10) shows that the fore legs are already visible through the skin, although they are not to be seen in the normal specimen at this age. The interest of the set of experiments lies in the clear demonstration afforded that the first effect of hyperthyroidism in the tadpole is upon the skeleton. Other parts of the body appear normal and the tissue of the thyroids and the grafts is of the normal sort, showing no hypertrophy.

III. *Transplantation of the thyroid to the tail.* A still further proof of the relation of the thyroid to skeletal development is given by the third set of operations. In these the thyroid anlage was taken out of its normal position and planted in the tail. The animals developed normally up to the maximum length. When they had reached the stage just preceding metamorphosis, the tails, including the thyroid grafts, were cut off, thus removing the gland after it had functioned for some time. The plan was to see if the tadpoles which had had their thyroids through the period of skeletal development could complete metamorphosis in the absence of the gland. Two facts are demonstrated by these experiments. One is that the thyroid is not directly necessary for the later stages of metamorphosis if it is present till the animal has reached its maximum size. The other is that the presence of a graft in the tail greatly increases the likelihood of regeneration of thyroid in the normal situation. In other thyroidectomy experiments the percentage of regeneration has been from two to ten per cent, while among the animals with thyroid grafts seventy-five per cent showed regeneration of the gland in the normal situation. Microscopic examination of specimens showed that the condition may vary all the way from that of an animal in which the graft in the tail has been resorbed and the gland has regenerated in the normal position, to that in which there is a large graft in the tail and no thyroid tissue remaining in the body after the second operation. There seems to be a connection between the development of the graft and the regenerated gland. When the latter is large and healthy, the graft is usually resorbed. The grafts in those animals in which there was no regeneration were all large, and some of them showed a marked hypertrophy with tall columnar epithelium and very large irregular follicles.

DISCUSSION

The results obtained from the experiments described fall under two heads: the relation of the amount and kind of thyroid tissue to the rate of development, and the relation of the gland to different phases of metamorphosis. *Precocious metamorphosis and delayed metamorphosis have been noted by other observers* occurring naturally among the tadpoles kept in the laboratories. Jensen (1921) has made a study of a few such cases. He reports that out of seven cases of precocious metamorphosis four show enlarged thyroids and three do not. One gathers from the illustrations, however, that the three animals in which the thyroids were said to be small were themselves below the normal size, and it seems at least possible that the glands were relatively large. No hypertrophy is evident from the figures. Probably, however, some other factor than the size of the thyroid is involved in the production of precocious frogs. We have never been able, in spite of repeated attempts, to induce metamorphosis more than two weeks ahead of the normal time, except in the single instance already described. The size of the gland has some effect on the rate of development, but the effect in the precocious frog seems disproportionate to the amount of hyperplasia.

The possibility that the thyroid is concerned chiefly with the skeletal changes of metamorphosis has already been suggested by us and by Allen (1919). Allen notes that in *Bufo* the limb development and the disappearance of the tail follow the accumulation of the colloid in the thyroid; but since the tail disappears during the period when there is actual diminution of the gland, he suggests that this feature of metamorphosis is independent of the thyroid. The other possibility is that it may occur as the result of the accumulation of a considerable amount of colloid, though no more is added while it takes place. The experiments which we planned in 1919 to test this particular point are not absolutely conclusive by themselves. Metamorphosis may be completed after complete removal of the thyroid, if this removal takes place when skeletal development is well advanced, but there is the possibility that it does so through the agency of hormones remaining in the body after the gland has been removed. The period during which the animal continues to develop normally after the removal of the thyroid is

not a very long one (about three weeks) and it is possible that if the process of metamorphosis had lasted longer a different result would have been obtained. The results of other transplantation experiments, however, favor the view that the skeletal changes of metamorphosis are the only ones to be influenced by the thyroid, for in them we saw that the result of hyperthyroidism was visible in the shape of the head and the development of the fore limbs while the shrinkage of the tail and the viscera were delayed until the normal time of metamorphosis.

SUMMARY

1. The epithelium of regenerating thyroid glands may undergo hypertrophy, resulting in abnormally shaped follicles lined with tall columnar epithelium. A very small amount of this abnormal tissue is sufficient to cause the animal to develop at the normal rate.

2. In the absence of this hypertrophy, the rate of development varies with the size of the regenerated gland.

3. Precocious metamorphosis was not caused either by allowing the thyroid to regenerate or by engrafting additional thyroid tissue. Although precocity is accompanied by a relatively large thyroid, it is probable that some other factor is involved in its production.

4. The effect of the presence of grafts of thyroid tissue is visible only in an advance of skeletal development. Metamorphosis is not hastened by the operation.

5. The results of these experiments illustrate the difference between the effect of thyroid feeding and of hyperthyroidism.

6. Animals which are deprived of their thyroids just prior to the normal time of metamorphosis, when the skeletal development is well advanced, are able to complete the transformation to the adult form. It appears that the later changes of metamorphosis are independent of the thyroid.

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PLATE 1

Figure 1. Tadpole with regenerated thyroid: development retarded.

Figures 2-4. Tadpoles with regenerated thyroids: development normal.

Figure 5. Precocious frog.

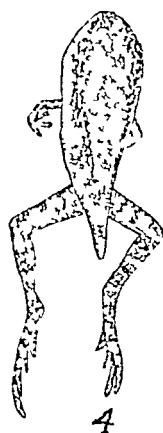
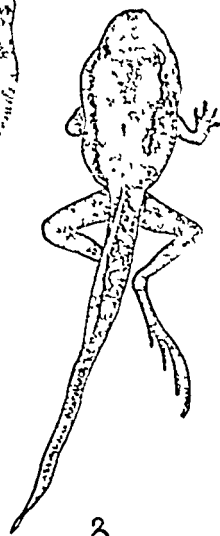
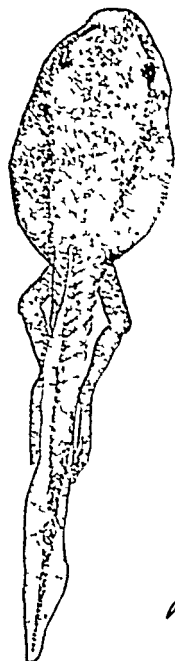
Figure 6. Thyroidless tadpole.

Figure 7. Normal tadpole at maximum.

Figure 8. Tadpole with thyroid graft.

Figure 9. Lateral view of tadpole with thyroid graft.

Figure 10. Ventral view of same.



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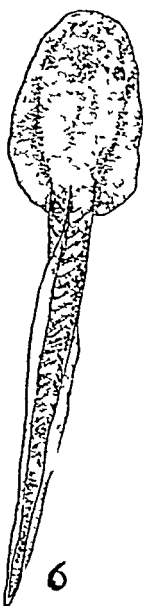
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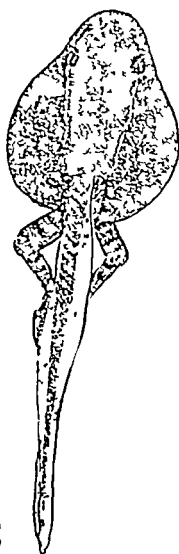
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PLATE II

Figure 11. Regenerated thyroid showing hyperplasia.

Figure 12. High power drawing of the same.

Figure 13. Group of follicles from normal thyroid (same magnification as Fig. 11).

Figures 14 and 15. Epithelium of normal thyroid showing limits of variation in the height of the cells.

Figure 16. Epithelium of regenerated thyroid in which there was no hyperplasia.

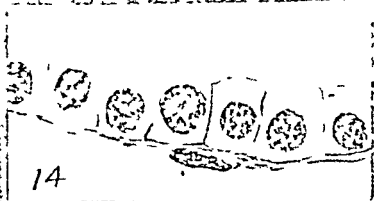
Figure 17. Follicles of small thyroid without hyperplasia (largest section of the gland).



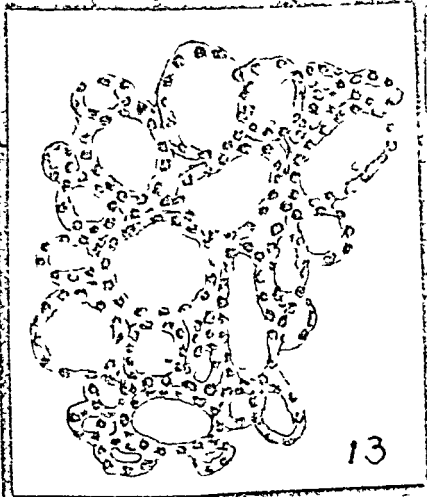
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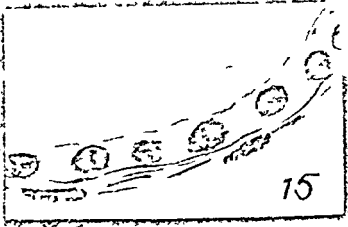
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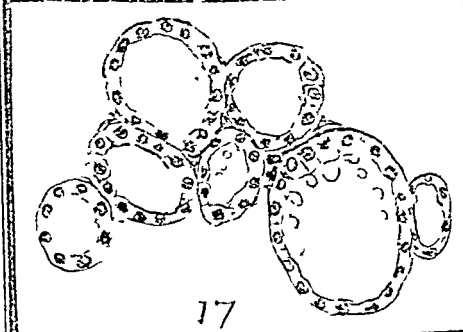
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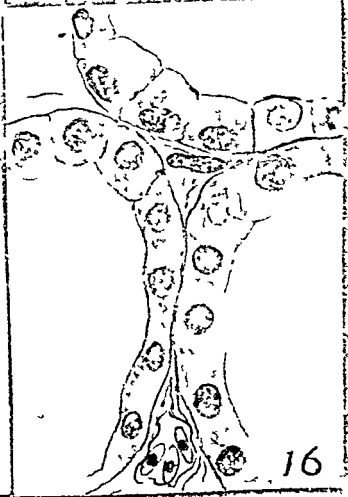
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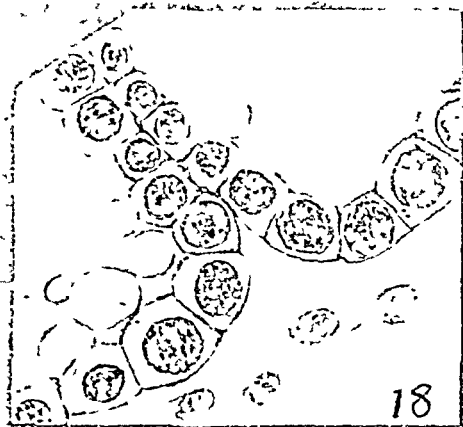


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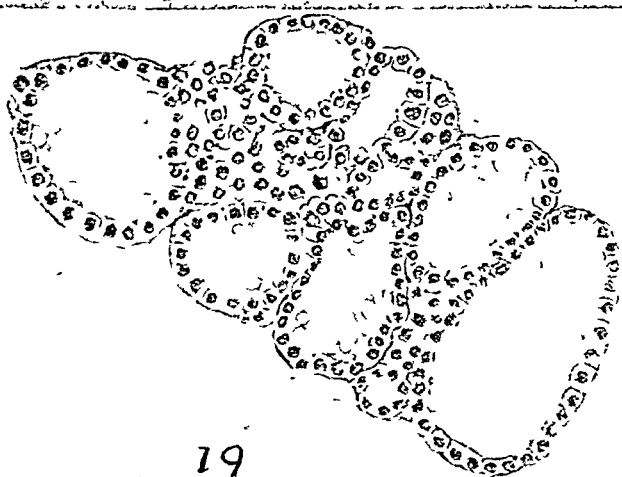
PLATE III .

Figure 18. Epithelium from thyroid of precocious frog.

Figure 19. Largest sagittal section of thyroid of precocious frog.



18



19

THE EFFECT OF THE ABLATION OF THE SUPERIOR CERVICAL SYMPATHETIC GANGLIA UPON THE CONTINUANCE OF LIFE

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Some recent work by Meltzer (1920) on the ablation of the superior cervical sympathetic ganglia indicates that certain common laboratory animals do not survive the removal of these bodies. This careful investigator found in a large series of animals that approximately 90 per cent of his experimental animals succumbed in from one to ten days to this operative procedure, exhibiting on death pulmonary lesions. It was suggested by this worker that these results may have been due to an endocrine function exercised by these ganglia.

These results, whatever may have been the cause of death, are at variance with somewhat similar work of other investigators. E. Sharpey Shafer (1919) demonstrated before the English Physiological Society two rabbits, each of which had had its superior cervical sympathetic ganglia removed in two operations a week apart, one ganglion being removed at each operation. These animals were alive weeks after the last operation had been performed. In man removal of the superior cervical sympathetic ganglia as a means of alleviating the distressing exophthalmic symptoms of goiter was suggested and practiced by Jaboulay (1896). Mayo (1914) and others have used this operation on man with no apparent untoward effects. There has, however, been no systematic attempt in this work to determine whether ablation was complete. Mayo's paper is the most illuminating, as it contains figures showing the location and the exposure of the ganglion. He seems to have no doubt that removal was complete in several cases but, obviously, histological proof of removal could not be offered.

As Meltzer's is the most extensive work so far performed for the distinct purpose of demonstrating the effects upon life of ablating these ganglia, it deserves a fuller review at this time.

His series comprised twenty-eight rabbits and three cats. Six of his rabbits died in less than 24 hours, nine in less than two days, five in less than three days, and five others within ten days of the operation. Two cats died within two days. All of these animals at autopsy showed pronounced pulmonary lesions. Three rabbits and one cat survived. These four animals were examined by his physiological test (the "paradoxical" eye reflex test). One rabbit and the cat gave a negative test, which was taken to indicate that ganglionic tissue was present. The remaining two rabbits gave a positive test. The survival of these animals Meltzer has attributed to the possible presence of a minute amount of ganglionic tissue.

Because of the divergence between the results of Meltzer's work and that of other investigators it was felt that the subject deserved a careful re-examination.

In my work three types of experimental animals were used, namely, rats, rabbits, and cats. The rats were of young, healthy stock, especially selected. Young as well as old rabbits were purposely chosen for the work. The cats also varied considerably in age as will be seen from the tables. Great care was taken in the hygiene and care of the animals. The operative work was done during the months of February and March, 1921.

OPERATION

After exposure of the upper portion of the vago-sympathetic chain the sympathetic was carefully separated from the vagus in the cephalic direction until the superior ganglion was reached. This ganglion was then separated from the adjoining vagus ganglion. In effecting this separation considerable difficulty was experienced in the cats in which form, as is well known, the two ganglionic bodies are intimately associated. In the rats this association is less intimate, while in rabbits they are definitely separated. In no form did this association preclude a complete separation of the two ganglia, and the ablation of the sympathetic ganglion as was subsequently determined by histological study (see table). After this separation had been effected the dissection was carried further cephalad until the upper sympathetic roots were found. These fibers were then carefully pulled loose from their cephalic attachments, the sympathetic nerve sectioned about a centimeter below the ganglion, and the latter removed.

76 ABRATION OF SUPERIOR CERVICAL GANGLIA

All of my animals recovered, save one cat, which showed continued signs of snuffling and finally died eleven days after the operation. After recovery from the immediate effects of the operation, except for this one animal, no ill effects upon the

		Age	Sympathetic ganglionic tissue; histological examination		Time between operation and sacrifice of animals	Condition of lungs	"Paradoxical" eye reflex test
			Right side	Left side			
Rat	1	117 days	Present	Present	17 days	No examination	No examination
Rat	2	120 days	Absent	Absent	14 days	No examination	No examination
Rat	3	120 days	Absent	Absent	14 days	No examination	No examination
Rat	4	100 days	Absent	Absent	20 days	No examination	No examination
Rat	5	100 days	Absent	Absent	20 days	No examination	No examination
Rat	6	100 days	Absent	Absent	20 days	No examination	No examination
Rat	7	107 days	Absent	Absent	19 days	No examination	No examination
Rat	8	107 days	Absent	Absent	19 days	No examination	No examination
Cat	102	Young female	Absent	Absent	56 days	Consolidated areas right lung	Positive
Cat	103	Male 1 year	Absent	Absent	58 days	Normal	Positive
Cat	104	Six months	Doubtful*	Absent	68 days	Normal	Positive
Cat	105	Eight months	No examination	No examination	11 days Died	Congestion lower half both lungs	No examination
Cat	106	Old animal	Absent	Absent	40 days	Normal	Right positive, left blind
Cat	107	Old animal	Absent	Absent	38 days	Normal	Negative
Rabbit	1	Old animal	Present	Present	49 days	Congestion and acriation upper right	Positive
Rabbit	2	Young animal	Absent	Absent	42 days	Normal	Positive
Rabbit	3	Young animal	Absent	Absent	39 days	Normal	Positive
Rabbit	4	Young animal	Absent	Absent	30 days	Normal	Positive

*A group of nerve cells were found whose connections were doubtful though the examination seemed to indicate than sympathetic.

health of any of the animals were noted. The animals, however, showed the eye effect characteristic of sympathetic section.

PHYSIOLOGICAL TEST OF RESULTS

Not less than 48 hours after the operation the cats and rabbits were tested for removal of the sympathetic ganglia by the "paradoxical" eye reflex method (Meltzer, 1904; Meltzer and Auer, 1904). (The difficulty of seeing the pupil prohibited this test in the rat.) The test consists of instilling adrenalin, 1:1000, into the eye or of injecting 1 to 3 cc. of adrenalin, 1:1000, subcutaneously. The instillation method works well on rabbits, while the injection method is the most satisfactory for cats. Distinct dilatation of the pupils with this treatment indicates a complete removal, according to Meltzer (1904).

Thus, sectioning of the sympathetic nerve or an incomplete removal of the superior cervical sympathetic ganglion did not elicit a positive response (test); complete removal did elicit such a response, according to this investigator. In his latest work, Meltzer (1920) admitted that two of his animals which gave the paradoxical response survived and because of this he was inclined to believe that a positive response does not necessarily mean a complete ablation, though it does show a nearly complete removal.* It must be recognized, however, that Meltzer's conclusions are not supported by microscopical examination of the tissue of this region for ganglionic remnants.

All of my cats and rabbits were examined by the "paradoxical" eye reflex test, and all of them except cat No. 107 showed dilatation of the pupils. Histological examination demonstrated the absence of any ganglionic tissue in this animal.

The suggestion given by Meltzer (1904) that when using the subcutaneous method, the dosage should be 1 to 3 cc., varying with the size of the animal, may throw light upon the results obtained with the above mentioned animal (cat No. 107) when submitted to the eye test. Two cc. were used on this cat, which was an unusually large animal, and no doubt the dosage was too small to elicit the dilatation response. I may say, therefore, that although the test may help demonstrate successful ablation,

* One of my animals seems to lend support to this contention, for rabbit No. 1, though giving a positive eye test, showed histologically the presence of quite a definite amount of sympathetic ganglion tissue on each side.

as it is used at present, it seems that it cannot be counted upon to give any absolutely conclusive results.

AUTOPSIES

Proof of ablation then must be histological and not physiological, and it would seem, as previously stated, that it is unfortunate that Meltzer must admit that in his work "no macroscopical or microscopical examination" was made. In my work the animals after the operation were permitted to live for a period of two weeks to two months. They were then killed and autopsied. Especial attention was given to the lung examination, and to an examination with the binocular microscope of the region of operation for the purpose of detecting any remaining ganglionic tissue gross and distinct enough to be determined by this means. The carotid artery and vagus nerve were then picked up and sectioned well below the region of the vagus ganglion. Dissection of these structures, together with all surrounding connective tissue, was carefully carried to the base of the cranium, from which all connective tissue was loosened. The carotid and vagus were cut as they entered the cranium, and the tissue was then removed and fixed in 10 per cent formol. Microscopical examination was made upon all of the animals reported save one (see table). This examination showed complete ablation of the ganglia from seven rats, four cats and three rabbits, all of which survived. With the exception of cats No. 102 and No. 105 and rabbit No. 1, the lungs of all of these animals were normal.

DISCUSSION

The conclusion, then, seems inevitable that the death of Meltzer's animals was not due to the complete ablation of these ganglia. For, as must be emphasized, all of my experimental animals save one survived, and this animal seemed never to recover from the immediate effects of the operation. Autopsy showed pulmonary lesions. It would appear, therefore, that Meltzer's two surviving rabbits more nearly represent the effects that can be expected from complete ablation than do the twenty-five animals which succumbed, death supposedly being due to the loss of the ganglia.

That the lesions found by Meltzer were not due to vagal interference is shown by the careful controls which he made to

cover this point. In advancing an explanation for the cause of the death of these animals he states, "From the foregoing evidences, I am inclined to conclude that the death of the animals in which both ganglia were removed was due to the removal of these organs—if I may call them so—and not due to the procedure of the operation. In other words, the superior cervical ganglia contain a principle which is essential for the maintenance of life" (Meltzer, 1920).

The suggestion of Meltzer that the superior cervical sympathetic ganglia elaborate a principle essential to the maintenance of life was supported by a series of four rabbits whose ganglia had been pulled loose from their cephalic connections, but not ablated. In these experiments, in addition to leaving in place the ganglia which he had thus freed, he also transplanted two foreign superior cervical sympathetic ganglia from other rabbits to each of these animals. These four animals survived, which led him to conclude that the superior cervical ganglia might elaborate an essential endocrine substance. All the evidence gathered from my own work speaks against this conclusion. Nor does the ascribing of a specific endocrine function to any part of the sympathetic system find support when the embryological development of this system in general is considered (Keibel and Mall, 1912), for we see from such a study that the whole system develops similarly from the neural crest. If, therefore, we are to ascribe an endocrine function to one part of the system it is hardly logical to deny the same function to the other parts. Accordingly, the removal of a single pair of these ganglia would not deprive the animal of a sufficient amount of this secretion to cause its death.

CONCLUSION

Our experiments on the ablation of the superior cervical sympathetic ganglia, which have been carefully checked up by histological study, have demonstrated that rats, cats and rabbits will survive their complete removal.

The fact that these animals survived complete removal of the ganglia argues against the conclusion that these bodies have an endocrine function essential to the continuance of life.

Embryological development of the superior cervical sympathetic ganglia does not seem to set them apart from the rest of

the sympathetic system as organs which might possibly have an obscure endocrine function.

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THE EPINEPHRIN CONTENT OF COMMERCIAL SUPRARENAL "CORTEX" PREPARATIONS

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As a result of the recent work on the thyroid-suprarenal cortex relationship (1) and more particularly that of Shapiro and Marine (2) and subsequently of others, the use of suprarenal cortex as one of the measures employed in the treatment of Graves' disease, is increasing. A number of commercial preparations of suprarenal cortex have recently appeared on the market.

It has been found that whole suprarenal gland, administered orally, causes nausea and vomiting in both man and lower animals. This is due to the epinephrin present. In view of the technical difficulties involved in separating cortex from medulla on a large scale and also because severe gastro-intestinal symptoms did result from the daily administration of 0.5 gram of a commercial suprarenal cortex preparation, it seemed advisable to determine whether these preparations contained significant amounts of epinephrin.

Shapiro and Marine used large doses of fresh suprarenal cortex (30 grams daily) or corresponding quantities of a glycerol emulsion, in the treatment of these patients. They found several desiccated preparations which they used comparatively ineffective. Nevertheless, it would, of course, be highly desirable to have a non-toxic, dry, active, stabile preparation available.

At least some, and probably all, of the products that can be purchased on the market are defatted by extraction with gasoline. This prevents them from becoming rancid. In the present state of our knowledge, however, it is a most pertinent question as to whether this extraction process does not remove or alter some physiologically active constituent of the glands. Further, since all of the marketed preparations examined contain considerable amounts of epinephrin, sufficient even in the small doses recommended (compared with those used by Shapiro and Marine, which are ten to thirty times as great) to cause untoward effects,

the advisability of using them at present is extremely questionable, especially in Graves' disease.

Seven specimens, purchased in different places and prepared by three firms, were examined for their epinephrin content by the method of Folin, Cannon and Denis (3) as modified by Seidell (4) for desiccated preparations. The analytical data are presented in Table I.

TABLE I

	Dosage Recommended	Epinephrin Content, Per Cent
Armour "Suprarenal Cortex, Desiccated," powder	1 to 3 grains	0.80
Armour "Suprarenal Cortex, Desiccated," tablets	three times a day.	0.41
Armour "Suprarenal Cortex, Desiccated," tablets		0.44
G. W. Carnrick "Suprarenal Cortex, Desiccated"	Average	1.09
G. W. Carnrick "Suprarenal Cortex, Desiccated"	dose 1 to 2 grains 3 or	0.97
G. W. Carnrick "Suprarenal Cortex, Desiccated"	4 times daily.	1.11
Marvell Pharmacal Co. Empco Brand Glandular Products "Adrenal Cortex"	Average dose 1 to 2 grains 3 times daily.	1.53

The amounts of epinephrin present vary from 4.1 to 8.0 mg. per gram of dry substance in the Armour preparations, 9.7 to 11.1 mg. per gram of substance in Carnrick preparations and 15.3 mg. per gram of substance in the Marvell Pharmacal Co. preparation.

In addition to these products, the so-called nucleoprotein of whole suprarenal gland, manufactured by Schiefflin & Co., according to Rogers (5), was analyzed and found to contain only traces of epinephrin.

If the doses recommended on the labels of the various products were used, the following amounts of epinephrin would be ingested daily:

Armour	0.8 to 5.8 mg.
G. W. Carnrick.....	2.6 to 5.9 mg.
Marvell Pharmacal Co.....	3.1 to 6.1 mg.

Whole desiccated ox suprarenal contains, according to Seidell (4), from 6.4 mg. to 9.1 mg. of epinephrin per gram of

substance (probably defatted), with an average value of 8.0 mg. per gram in four commercial preparations. Fenger (6) reports the average epinephrin content of 200 desiccated defatted suprarenal glands from full grown cattle to be 25 mg. per gram of substance and somewhat higher values in the case of young calves. From these data it is evident that only a partial separation of cortex from medulla has been effected in any of the preparations examined.

It is well known that the effect of the same dose of epinephrin on different persons varies greatly and that certain individuals are hypersensitive to very small doses even when given by mouth. The medical profession should, therefore, bear in mind that when prescribing the suprarenal cortex preparations now obtainable, they are recommending the ingestion of considerable amounts of epinephrin along with the glandular product.

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A CASE OF RAYNAUD'S DISEASE, RECOVERED

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Mr. A., a Hebrew of 39, was a truck driver up to the age of 23, later a tailor.

Family History: The father died at the age of 69, the mother at the age of 54; the causes of their deaths were unknown to the patient. One brother died from an accident; 4 brothers and 3 sisters were living and well. No disease similar to the patient's ever occurred in the family.

Patient's History: The patient's general health had always been good; he did not remember having had any childhood diseases; his boyhood had been exceptionally healthy and devoted to athletics. He married at the age of 25, but had no children. His head, eyes, ears, nose and throat had never caused him any trouble. He had no chronic cough and was not subject to colds. He was not easily tired. His appetite was fair, his digestion good, his bowels regular. He denies any venereal infection; he had no dysuria nor nocturia. He went to a Jewish school from the age of 4 to 13. He was of normal mentality. His habits were excellent (no alcohol, tea, coffee, or tobacco). He used to sleep very well and, whenever possible, for long hours; during his illness, however, his sleep was much disturbed by the pain he suffered.

Present Illness: In February, 1921, the patient began to experience a sort of an itching pain, as he describes it, in both hands. This pain, situated at first in the palms of both hands at the bases of fingers, later extended to the fingers themselves. It was not paroxysmal in character, but continuous, becoming progressively more and more intense.

There were no objective changes visible until four months later, when both hands became hyperemic, dark purple. Half a year later, that is, in August, 1921, the left third finger broke down and later the right thumb.

The patient was under morphia for several weeks before he came to see me. He changed residence and doctors frequently and late in September, 1921, came under my care.

Physical Examination: He was a well built, well nourished man (5 feet 5½ inches in height and weighing 150 pounds). He was very pale, almost muddy in color, evidently very exhausted, nervous and trembling. His pupils reacted to light and accommodation. His head, eyes, ears, nose and throat were normal. He had a bridge in the

mouth with two crowns. His gums were normal. The cervical glands and thyroid were not palpable. The lungs were normal to percussion and auscultation. The cardiac apex was in the fifth interspace $10\frac{1}{2}$ cm. from the midsternal line. The tones were clear, with no murmurs. P2: A2. The blood pressure was 98-70. The pulse was 96 and of a fair quality. There were no masses in the abdomen and no tenderness nor resistance. The spleen and kidneys were not palpable. The reflexes, especially the deep ones, were greatly exaggerated. There was no general glandular enlargement. His feet were perfectly normal. Both hands were markedly hyperemic, his fingers almost black-purple. The third left finger and right thumb were necrotic (dry necrosis). No distinct demarcation line was present.

Laboratory Findings: The urine was a clear, dark amber color, with a specific gravity of 1020 and acid reaction; it contained no albumen and no sugar. The Wassermann test was absolutely negative with all three antigens (plain alcoholic, cholesterinized and Noguchi's acetone insoluble). His blood tested: hemaglobin, 75 per cent (Sahli); erythrocytes, 4,800,000; leucocytes, 7,600. There was withdrawn 4 cc. of perfectly clear spinal fluid, colorless and under normal tension. The cell count was 4. The globulin was not increased. The Wassermann test was absolutely negative. A provocative dose of Neosalvarsan was given, followed by 3 consecutive negative Wassermanns.

Special Examinations: Ophthalmoscopic examination revealed a normal fundus.

Therapy: The patient was sent to Multnomah Hospital. He was given alcoholic benzyl benzoate gts. 20, t. i. d., for 3 days. He suffered intensely, crying from pain and sleeplessness. At the end of the third day he had a quite profuse hemorrhage and collapsed. His pulse was 160. The benzyl benzoate was discontinued. He was transferred to the Good Samaritan Hospital. Medium doses of Schlesinger's solution 4 to 6 times per diem were given. Passive congestion was applied twice a day for 4 weeks, later once a day. Wet dressing was applied.

The demarcation line became very pronounced. Very rapid progress was made with the fingers, but intense pain persisted, exaggerated to a marked degree by the application of passive congestion.

During the second week in the hospital Dr. Laurence Selling saw the patient in consultation. We agreed to tell the family that the case was practically hopeless and that all we could do was to keep him comfortable by relieving his pain with morphia.

During the second week in the hospital I decided to administer anterior pituitary substance in the hope of supplying the mysterious trophic stimulus so overabundantly furnished to the acral structures in cases of acromegaly. He was given 2 gr. t. i. d. The result was almost dramatic in effect. In but a few days the pain decreased to such an extent that the patient remained without morphia for days at a time. Occasional application of passive congestion, however, intensi-

fied the pain so that small doses of morphia were necessary, but during the fourth week morphia was abandoned entirely and after that recourse to it was not necessary.

The patient gained in appetite and craved bread particularly; $\frac{1}{4}$ gr. of thyroid was added during the fourth week.

All the fingers revived. The right thumb proved to be necrotic only as far as the soft parts were concerned and healed completely during the fifth week in the hospital. Necrosis of the third left finger involved the bone.

The patient left the hospital after 2 months. He gained over 20 pounds in weight (weighing then 174 pounds). He did not suffer the slightest pain, his blood pressure averaged 130-135 systolic, and 60-70 diastolic. His pulse was 72-76.

He slept a little too much, averaging some eleven hours, and was in splendid physical condition with the exception of his third left finger, which was still in the process of repair.

In January, 1922, the patient was presented to the Portland City and County Medical Society. His condition, with the exception of the third left finger, was perfect.

In March, 1922, the third left finger also healed, being shorter by about one-third of the terminal phalanx.

At the present time the patient is in perfect physical condition, has a constant weight, is working very actively and enjoying life generally.

Passive congestion had been discontinued with the healing of the fingers, but he is still on anterior pituitary and thyroid feeding. One could omit them and see what happens next, but the patient is as yet unwilling to try the experiment, the horrors of his intense suffering being too fresh and vivid in his memory.

Abstract Department

The effect of ADRENALECTOMY upon the total metabolism of the cat. Aub (J. C.), Forman (J.) & Bright (E. M.), *Am. J. Physiol.* (Balt.), 1922, 61, 326-348.

This paper deals with the basal metabolic changes which follow the extirpation of the adrenals. The work was undertaken with the object of studying more thoroughly the possible independent relationship of the adrenals to the control of the metabolic rate. The method of Benedict and Homans was used. A large volume of data is presented in the form of charts. Forty-eight hours after the removal of both adrenals in the cat there is a reduction of about 25% in the total metabolism without marked change in the relative percentages of foodstuffs burned. The removal of one adrenal causes a temporary fall, followed by a return to normal. Denervation of the remaining adrenal is followed by a slow fall in the metabolic rate. Evidence for the independence of the thyroid and adrenal effects upon the metabolic rate is discussed and the theory is suggested that the thyroid is the slowly acting regulator of the metabolic mechanism, while the adrenals control quick changes of short duration by variations in their secretion.—T. C. B.

ADRENAL bases, hyperglycemia and glycosuria (*Bases adrénalines, hyperglycémie et glycosurie*). Bierry (H.), Rathery (F.) & Levina (Mlle. L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1133-1135.

It was noticed that no glycosuria developed after the injection of certain salts of adrenalin and this led to a study of a number of adrenalin bases, both natural and synthetic. After the injection of certain adrenalines there may be notable hyperglycemia without the appearance of glycosuria. On the contrary, other adrenalines easily provoke glycosuria, but not so marked as that described after the injection of the natural (levo) adrenalin of Bertrand.—T. C. B.

Variations of protein sugar after injection of ADRENIN (*Variations du sucre protéidique après injection d'adrénaline*). Bierry (H.), Rathery (F.) & Levina (Mlle. L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1135-1137.

In studying the effect of adrenalin on glycemia the authors have limited their observations to the free sugar. This paper deals with the protein sugar. Injections of various adrenalines were made into

dogs, and a comparative examination of the concomitant variations in free sugar and protein sugar, using the method of Bertrand, were made. On the whole, the variations of the two kinds of sugar are in the inverse sense; the diminution of the protein sugar at the beginning of the action of adrenalin coincides with the maximum of free sugar in the plasma. Tables of results are given.—T. C. B.

The metabolic effect of ADRENALECTOMY upon the urethanized cat.

Aub (J. C.), Bright (E. M.), & Forman (J.), *Am. J. Physiol.* (Balt.), 1922, **61**, 349-368.

There is considerable evidence that adrenin is secreted more rapidly under urethane than in the animal with no anesthesia. Therefore, a series of experiments were made on urethanized cats, as it seemed possible that the effects of adrenalectomy on metabolism might be more readily observed. Many tables are given, and the evidence suggests a greater flow of adrenalin under urethane anesthesia than normal. After removal of the adrenals under urethane there is a prompt fall of metabolism averaging 12 per cent; this drop also occurs after removal of the thyroid, showing that this latter gland is not essential to the reaction. Intravenous injection of adrenalin at a physiological rate causes a rise in metabolism. It is suggested that the fall in metabolism is due to an absence of the adrenal secretion.—T. C. B.

(ADRENAL) Oedema in food-deficiency diseases. Bigland (A. D.), *Lancet* (Lond.), 1920, **i**, 243-247.

The paper deals with many outbreaks of epidemic dropsy during the late war, associated with various pathological and especially dietary conditions. Malnutrition (lack of vitamins, etc.) leads to hypertrophy of adrenals (McCarrison) and thus to oedema. Hyperactivity may in time lead to adrenal insufficiency, just as exophthalmic goiter gives place to myxedema. Pellagra is considered to be an example of this.—Physiol. Abst., **5**, 31.

Action of ADRENIN on the respiratory exchange and nitrogen of 24 hours. Importance of the method of administration (*Action de l'adrénaline sur les échanges respiratoire et azotés des 24 heures. Importance de la voie d'administration*). Bru (P.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 1068-1069.

Adrenalin, administered subcutaneously, increases oxygen consumption by as much as 31 per cent, while if given by mouth it causes a slight decrease. The excretion of nitrogen is not modified.

—T. C. B.

The production of ADRENAL discharge by piqûre. Carrasco-Formiguera (R.), *Am. J. Physiol.* (Balt.), 1922, **61**, 254-271.

The experiments were done on cats and the denervated heart was the index to increased adrenal secretion. Puncture of the floor

of the fourth ventricle increased the rate of the denervated heart even when the hepatic factor was eliminated by section of the hepatic nerves. Increased heart rate did not occur if the venous path from the adrenals was blocked. It was concluded that "piqûre" produced discharge from the adrenals of a product that reached the arterial blood in sufficient amount to exert on other organs an effect identical with that of adrenalin.—T. C. B.

SUPRARENAL gland in anesthesia. Corbett (J. F.), J. Am. M. Ass. (Chicago), 1922, 79, 543-545.

Corbett seeks a condition common to those patients who react badly under ether anesthesia, as noticed particularly in typhoid fever, all severe infections, starvation, late intestinal obstruction, shock, secondary anemia due to hemorrhage, exophthalmic goiter, and in prolonged etherization itself. The common condition, according to his research, is epinephrin exhaustion. Epinephrin is necessary to maintain vasoconstriction, which in turn is essential to the maintenance of proper blood pressure and circulation where the blood volume is small. When the epinephrin output is exhausted the vascular system decompensates and death ensues. The study entailed the determination of the residual epinephrin in the suprarenal gland in animals subjected to various procedures or dying from various causes. The determinations were made according to the physiologic standardization method of Elliot. Three hundred and fifty such experiments were done, the results being tabulated. In all cases the epinephrin content was less than one per cent of the normal. He does not believe that epinephrin exhaustion is shock, but that the exhaustion is the cause of final collapse.—W. M. A.

An anomalous arterial supply to SUPRARENAL, kidney and OVARY. Dawson (A. B.) & Reis (J. H.), Anat. Record (Phila.), 1922, 23, 161-167.

Certain anomalies of the arterial system in a full term female fetus are described. They are interpreted as supporting Bremer's claim that the renal, suprarenal, and sex-gland arteries are derived from an early periaortic plexus. The article is not of immediate endocrine interest.—W. J. A.

(ADRENALS) Restriction hyperglycemia and glucosuria in rabbits. Fujii (I.), Tohoku J. Exper. Med. (Sendai), 1922, 2, 531-561.

The seasonal variations of restriction hyperglycemia in rabbits are not influenced by the external temperature nor the degree of coolness of the room temperature. The degree of the glucosuria is influenced on the one hand by the external temperature and on the other it is dependent upon the degree of hyperglycemia. The glycogen content of the liver of rabbits in the winter and spring is reduced by a one day fast to a third of the normal; a two day fast reduces it to a quarter of its normal value.—F. S. H.

(ADRENAL) Addison's disease with vasomotor phenomena, particularly of the fingers (*Maladie d'Addison avec phénomènes vasomoteurs particuliers des doigts*). Hanns, Soc. Méd. du Bas-Rhin, 1922, July 24; abst., *Presse méd. (Par.)*, 1922, 30, 694.

The author reports a case of Addison's disease with little pigmentation, relatively moderate asthenia and very great hypotension. When the abdomen was palpated a tumor was found which autopsy showed to be the adrenal capsule, increased in volume by tuberculosis infiltration. Besides, there was a series of accessory symptoms: contraction of the muscles of the thigh, central and peripheral hypothermia except in the abdomen, uneven pupillary movement of sympathetic origin, ocular hypotonia, extreme dilatation of the pupil after the instillation of cocaine, diminution of urinary acetone, decrease of glycemia and marked vasomotor troubles consisting in paleness of the fingers following immersion of the hand in cold water. Oscillations of the radial and of the humeral arteries underwent about the same modifications. The significance of these phenomena is the same as that of the line of Sergent and is explained by vasomotor hyperexcitability due to defective functioning of the sympathetic.—R. G. H.

The emergency functions of the ADRENAL. Hartman (F. A.), *Science (N. Y.)*, 1922, n. s. 56, 146-147.

The iris on one side was sensitized to epinephrine by removal of the superior cervical ganglion. The ciliary ganglion was removed in order to eliminate central nervous influence. It was found that stimulation of the moist pinna by rapidly repeated induction shocks caused a dilatation of the denervated pupil. Asphyxia caused almost maximal dilatation. Exposure to cold caused a marked dilatation. After removal of both adrenals, induction shocks, asphyxia and cold caused little or no effect on the denervated pupil.—F. A. H.

(ADRENAL) SUPRARENAL support in phenol poisoning. Hayes (C. F.) & Horn (W. S.), *Texas State J. M. (Ft. Worth)*, 1922, 18, 218.

A case in which a patient, comatose and apparently moribund two hours after swallowing one ounce of carbolic acid, was given 20 minims of adrenalin hypodermatically. This was repeated every two hours for eighteen hours. Recovery was complete.—C. R.

Influence of the ADRENAL cortex upon the health and growth of various organisms (*Der Einfluss der Nebennierenrinde auf Gesundheit und Wachstum verschiedener Organismen*). van Herwerden (M. A.), *Biol. Zentralbl.*, 1922, 42, 109-112.

One to two milligrams of dried adrenal cortex tissue when added to 10-15 cc. of hay infusion containing *Daphnia pulex* stimulated growth and accelerated the maturing and reproductive proc-

esses. Similar stimulation of growth was observed with the eggs of the snail (*Limnaea ovata*) and with frog larvae (*Rana esculenta*). In the case of tadpoles, larger and stronger larvae were produced than in those fed hypophysis extract. Neither hypophysis nor adrenal extracts had any effect upon the metamorphosis of the tadpoles. The general favorable influence of small quantities of adrenal cortex upon the nutrition of animals is emphasized.—Chem. Abst., 16, 2937.

The functions of dogs deprived of the ADRENAL medulla (*Les fonctions des chiens privés de la substance medullaire surrénale*). Houssay (B. A.) & Lewis (J. T.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 565-567.

Of 9 dogs from which the suprarenal medulla on the left side was destroyed, and the right entire gland removed, 5 survived, and appeared normal. There was no asthenia; the pulse, respiration and temperature were normal. The wound cicatrized perfectly. One month after the second operation the injection of adrenalin or of extract of hypophysis caused a rise of pressure similar to that of the controls. Mydriasis of the same intensity and duration as in the controls was obtained by instillation of cocaine, atrophine and adrenalin. The composition of the blood was normal. There were no pigment changes. No changes were found on autopsy, except a cicatrix occupying the place of the entire medulla of the left suprarenal. There was no trace of suprarenal on the right side, and no accessory glands. It seems that complete destruction of the suprarenal medulla is compatible with a normal state, while the cortex is of importance *quo ad vitam*.—T. C. B.

(ADRENAL) Addison's disease, with severe anemia, treated by suprarenal grafting. Hurst (A. F.), Tanner (W. E.) & Osman (A. A.), *Proc. Roy. Soc. Med. (Lond.)*, 1922, 15, 19-20.

Details of a partially successful case.—A. T. C.

The antagonism between histamine and ADRENALIN. Kellaway (C. H.) & Cowell (S. J.), *J. Physiol. (Lond.)*, 1922, 56, xx-xxi.

The intravenous injection of small doses of histamine causes slowing of the heart, dilatation of the pupil, sweating and salivation, but in addition there is a rise in the hemoglobin percentage of the venous blood, which, in normal cats passes off in 20 to 30 minutes. In cats dying of adrenal insufficiency there is a similar, or greater concentration and the effect persists for several hours. In the animals upon which these observations were made one pupil had been denervated by excision of the superior cervical ganglion, and responded preferentially. During this response small doses of histamine caused either little or no concentration of hemoglobin. Animals with marked adrenal insufficiency are often prostrated by a minute dose of histamine, but this does not occur if adrenalin is first

administered. The authors hope later to differentiate the part played by medulla and cortex in these phenomena.—T. C. B.

(ADRENALS) Addison's disease; report of case. Koo (U. K.), Nat. M. J. China (Shanghai), 1922, 8, 120.

Reference cited from J. Am. M. Ass., 79, 999.

ADRENAL therapy. Lawrence (C. H.), Boston M. & S. J., 1922, 187, 168-169.

This paper gives a very brief summary of the conditions in which extracts of the adrenal may be useful. It closes with a warning against indiscriminate adrenal therapy. There is no new information.—J. C. D.

ADRENAL disturbances in infantile pathology, particularly acute adrenal insufficiency (*Les troubles des surrénales en pathologie infantile et spécialement l'insuffisance surrénale aiguë*). Lereboullet (M.), Progrès méd. (Par.), 1922, 37, 199-202.

One of a series of lectures. Generalized discussion.—F. S. H.

Chronic ADRENAL insufficiency and Addison's disease in childhood (*L'insuffisance surrénale chronique et la maladie d'Addison chez l'enfant*). Lereboullet (M.), Progrès méd. (Par.), 1922, 37, 210-212.

One of a course of lectures. No new data.—F. S. H.

Studies of the function of the ADRENALS by means of the functional survival method, together with the production of a cardinal symptom of Addison's disease (*Beiträge zur physiologie der Drüsen. Mitt. 50* Asher, L. *Untersuchungen über die Funktion der Nebennieren mit Hilfe der funktionellen Ueberlastungsmethode, und über die Erzeugung eines Kardinalsymptomes des Morbus Adisonii*). Mauerhofer (E.), Ztschr. f. Biol. (München u. Leipz.), 1922, 74, 147-172.

The adrenals can be removed from the rat and the animal will survive. This, however, fails to give data concerning the function of the adrenals in this animal. Nevertheless, if adrenalectomized rats are made to do work it is found that they become tired and exhausted much more quickly than do normal animals. The recovery from fatigue is also much slower and much less complete. Hence, it was possible to reproduce a cardinal symptom of Addison's disease. The possible replacement value of accessory adrenal tissue is discounted in these experiments, inasmuch as the adrenalectomized rats exhibited extreme fatigue after exercise even though the so-called accessory tissue was present. Hence this latter can be but of minor importance. Attempts to carry on similar studies on guinea-pigs were generally unsuccessful, because the animals died after adrenalectomy.—F. S. H.

The action of the ADRENAL lipoids in epilepsy (*Sur l'action des lipoides surréniaux dans l'épilepsie*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 58-63.

The intravenous injections of adrenal lipoids is reported to have caused the seizures of epilepsy to be less frequent and less severe during the administration of the preparation.—F. S. H.

Changes in the ADRENAL capsule in insane pellagrins (*Sur les alterations des capsules surrénales chez les aliénés pellagres*). Parhon (C. J.) & Savini (E.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 6-11.

The adrenals in pellagra are frequently found sclerosed. Nevertheless the lesion is far from constant in appearance.—F. S. H.

Three cases of adenoma of the ADRENAL cortex (*Trois cas d'adénomes cortico-surrénaux*). Parhon (C. J.) & Stocker (A.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 12-17

Two of the cases reported were associated with the syndrome of hirsutism.—F. S. H.

The treatment of alopecia with ADRENAL lipoids (*Sur le traitement opothérapique surtout par les lipoids surréniaux dans un cas de pelade du cuir chevelu et des sourcils*). Parhon (C. J.) & Jacoby (D.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 77-84.

The case is described of a young lady of 20 years giving a history of scarlet fever, fright and malaria. There was marked alopecia. The thyroid was slightly enlarged. A preliminary attempt to induce hair growth by thyroid medication was unsuccessful. The injection of 0.03 grams of adrenal lipoids every other day and the ingestion of 0.25 grams of desiccated thyroid gland was followed by a good growth of hair.—F. S. H.

Studies in experimental traumatic shock. IV. The liberation of EPINEPHRIN in traumatic shock. Rapport (D.), Am. J. Physiol (Balt.), 1922, 60, 461-475.

Conflicting results and opinions as to the relation of the adrenals to traumatic shock led to the experiments here reported. Cats were used and shock induced by crushing the hind limb, the denervated heart being used as an indicator of adrenal activity. Full data are given in the form of tables, and a discussion of the results. In six out of nine cases there was evidence of hyperactivity of the adrenal glands during the development of traumatic shock. There was not sufficient reason to believe that either oversecretion of the adrenals, or their exhaustion, was a factor in the production of shock. It is probable that over-activity of the glands, in the development of shock, is a concerning factor.—T. C. B.

An undescribed relation of the SUPRARENALS to OVULATION.

Riddle (O.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 280-282.

The observations described here were made on pigeons, and make it extremely probable that the adrenals regularly and greatly enlarge in close relation to the time of liberation of ova from the ovary. The maximum size seems to be attained in the 44-hour interval between the ovulation of the first and second ova. The early stages of adrenal enlargement are coincident with the 4 to 5 days of extremely rapid growth which the ova undergo just before their expulsion from the ovary. Before undertaking the present study it had been found that birds which died of tuberculosis or from the presence of round worms usually showed enlarged adrenals.

—F. S. H.

(ADRENALS) Subsequent course of a case of Addison's disease.

Rowntree (L. G.), J. Am. M. Ass. (Chicago), 1922, 79, 556-557.

The late Dr. A. L. Muirhead described his own, a typical case, under the heading "An autographic history of a case of Addison's disease" (J. Am. M. Ass., 1921, 76, 652). The disease developed after a unilateral nephrectomy. Rowntree reports the subsequent course of events. Epinephrin and whole suprarenal gland therapy proved very efficacious temporarily, resulting in even temporary clearing up of the pigmentation. Intrarectal administration proved efficacious but was discontinued on account of tenesmus. The results justify a thorough trial of similar treatment in other cases of Addison's disease.—W. M. A.

(ADRENALS) The white line of Sergent (La ligne blanche cutanée, dite surrénale). Sézary (A.), Ann. de méd. (Par.), 1922, 11, 403-415.

The result of the studies of Sézary lead him to conclude that there is but one white line of the skin, and that is the physiological one described by Macey in 1858. It is observed in both well and diseased persons. Whether isolated or associated with asthenia or arterial hypotension, this white line has no relation to adrenal insufficiency.—F. S. H.

Ablation of an ADRENAL for hyperfunction (Exstirpation bei Hyperfunktion einer Nebenniere). Stephan & Flörcken, Wien. klin. Wchnschr., 1922, 35, 664; Deutsche med. Wchnschr. (Berl.), 1922, 48, 929.

In two cases of hypertension ablation of an adrenal produced only a fall of the number of erythrocytes. After the operation the patients showed an increased disposition to pigmentation of the skin. In one case in which the adrenals were exposed to x-rays, postmortem examination showed a reduction of the cortex. The chromaffin system was not altered.—J. K.

Morphine hyperglycemia and the ADRENALS. Stewart (G. N.) & Rogoff (J. M.), *Am. J. Physiol. (Balt.)*, 1922, 62, 93-112.

Hyperglycemia is less commonly induced by morphine in cats which have recovered from "complete" operations on the adrenals than in normal cats, or cats which have recovered from such operations as splenectomy. When hyperglycemia occurs in cats after adrenal operations it is less marked and more slowly reached. Dogs and cats behave in the same way. It is thought that morphine hyperglycemia is not an "adrenalin-hyperglycemia" due to stimulation of the glands, but that the ordinary output facilitates its production.—T. C. B.

ADRENAL-PANCREAS relations. I. Adenoma of the adrenal cortex and the islands of Langerhans (Relations surrénopancréatiques. I. L'adénome cortico-surrénal et les îlots de Langerhans). Stocker (A.), *Bull. et mém. Soc. neurol., psychiat., et psychol. de Jassy*, 1920, 2, 45-48.

A preliminary paper in which an attempt is made to establish an associative proliferation of the islands of Langerhans with adenoma of the adrenal cortex.—F. S. H.

The ADRENAL in experimental DIABETES (La surrénale dans le diabète expérimentale). Stocker (A.), *Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy*, 1921, 2, 100-103.

Report of the histological examination of the adrenals of 6 dogs which had been rendered diabetic by pancreatectomy. There was found a constant occurrence of an excess of lipid granules in the cortical zone.—F. S. H.

ADRENAL-PANCREAS relations. II. The experimental results (Relations surrénopancréatiques. II. Les données expérimentales). Stocker (A.), *Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy*, 1921, 2, 84-88.

Dogs were injected daily with gradually increasing doses of adrenin until 1 cc. was being given. This dosage was maintained until the experiment was terminated at 40, 50 and 60 days thereafter. The pancreas was removed and examined histologically. There were no noticeable modifications of the isles of Langerhans. The adrenal cortex was surcharged with an excess of lipoids.

—F. S. H.

The adrenalinemia following excitation of the splanchnic testifies to a secretory activity of the ADRENALS, governed by the nervous system L'adrénalinémie consécutive à l'excitation des surrénales, régie par le système nerveux. Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 776-778.

The process of physiological ADRENALEMIA: For and against (*Le procès de l'adrénalinémie physiologique: le pour and le contre*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 778-780.

Remarks regarding the communication of Tournade and Chabrol (*Remarques à propos de la communication de MM. Tournade et Chabrol*). Hallion (L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 780.

These articles are an answer to their critics and are controversial in nature.—T. C. B.

Influence of total decapsulation, then transfusion of ADRENAL venous blood, upon the arterial pressure; reality of a secretion of ADRENALIN without artificial excitation of the splanchnic nerve (*Influence de la décapsulation totale, puis de la transfusion de sang veineux surrénal, sur la pression artérielle; réalité d'une sécrétion d'adrénaline en dehors de toute excitation artificielle du nerf splanchnique*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 840-841.

In order to prove that adrenalin maintains arterial pressure, both suprarenals were removed from dog A. The blood pressure fell from 150 mm. Hg. to 80 mm. Meanwhile an anastomosis was made between the jugular of dog A and the right suprarenal vein of another dog, B, and the left suprarenal gland of dog B removed. On allowing the suprarenal blood of B to circulate in A, the pressure of A rose to 160 mm. Hg. The right splanchnic of B was then cut and the pressure of dog A fell to 100 mm. Hg. On stimulating the peripheral end of the same nerve, this pressure again rose to 160 mm. It is concluded that the suprarenal secretion plays an undeniable rôle in maintaining blood pressure and that the secretion is continuous through the tonic activity of the splanchnic.—T. C. B.

Revival of a decapsulated dog by transfusion of the venous blood of the ADRENALS (*Reviviscence d'un chien décapsulé par transfusion de sang veineux surrénal*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 842-843.

The experiment reported seems to demonstrate the reality of the internal secretion of the suprarenals and its powerful cardio- and angio-tonic action. After bilateral removal of the suprarenals in dog A, the blood pressure fell to 70 mm. Hg. in about 3 hours. While preparing a venous anastomosis of the jugular of dog A, with the right suprarenal vein of dog B, dog A apparently died. The blood pressure fell to zero, the heart and respiration stopped. No time was lost in transfusing from dog B, and in 30 to 40 seconds the heart began to beat and the blood pressure registered 45 mm. Artificial respiration for 5 minutes established a spontaneous respira-

tion which continued. The right splanchnic was cut and its peripheral end stimulated, and the blood pressure rose in dog B by pure vaso-constriction, more slowly in dog A by adrenalin secretion. When the nerve of dog B was not stimulated the pressure in dog A fell to 2 or 3 mm. and the dog "died" a second time. Excitation of the splanchnic again brought the pressure up to 48 mm. These facts testify to the existence of a physiological adrenalinemia.

—T. C. B.

Anastomosis of the ADRENAL with the jugular vein. Response to an objection of M. Hallion (*À propos de l'expérience d'anastomose veineuse surrénalo-jugulaire. Réponse à une objection de M. Hallion*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1137-1139.

A reply to his critics. Contains no new observations.—T. C. B.

Sudden death in infancy in consequence of acute ADRENAL insufficiency (*Über plötzliche Todesfälle im Säuglingsalter als Folge von akuter Nebenniereninsuffizienz*). Victor (M.), *Ztschr. f. Kinderh. (Berl.)*, 1921, 30, 44-54.

A report of two cases. A 14 months old boy was taken acutely ill with abdominal pain, irregular respiration, convulsions and rapid collapse. Death occurred 20 hours after the onset of symptoms. Necropsy showed hypoplasia of the left suprarenal with atrophy and calcification of the right. A 7 months old boy died during the night following the development of an extensive purpuric eruption. Necropsy showed hemorrhages into the skin and adrenals. In both cases Victor considers death as due to an acute adrenal insufficiency. In the second case this was due to hemorrhage. In the first case the insufficiency was due to atrophy following a probable hemorrhage into the gland at birth. The author does not consider ante-mortem diagnosis possible and doubts the possibility of effective therapy.

—C. H. G.

Effect of SUPRARENALECTOMY on nerves. Wertheimer (E.) & Duvillier, *Echo méd. du nord (Lille)*, 1922, 26, 229.

The excision of suprarenals in dogs and cats by Wertheimer and Duvillier demonstrated that the splanchnic nerve fibers inhibiting intestinal contraction possess an excitability independent from the one conferred by epinephrin in the blood.—J. Am. M. Ass., 79, 921.

Active and potential ADRENALIN (*Adrénaline active et adrénaline virtuelle*). Abelous (J. E.) & Soula (L. C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 749-750.

Adrenalin cannot be detected in the vena cava a short distance below the opening of the suprarenal veins. What becomes of it? The authors think it is not destroyed but only inactivated. It is

the amino group in adrenalin that is responsible for the rise of blood pressure and pupil dilatation, and there is some substance in the blood that inactivates this group, but does not destroy it. If $\frac{1}{2}$ mgr. of adrenalin is added to 10 cc. horse serum (hémostyl) and the enucleated eye of a toad put immediately into this mixture, dilatation of the pupil takes place in a few minutes. If, however, the mixture is allowed to stand for 45 minutes before the eye is put in, the mydriatic effect is completely suppressed. Such a mixture, if injected intravenously into a dog, immediately causes a strong rise of pressure; but if allowed to stand for an hour, double or triple the quantity will cause no rise. That the adrenalin is not destroyed is shown by the fact that when a fragment of muscle or pulpified intestine is added to inactive serum-adrenalin mixture, the pupil dilates as markedly as the control. The action on blood pressure is not so marked on account of the presence of a hypotensive substance in the extracts. This phase is being studied further. It is concluded that contact with blood serum causes adrenalin to lose its hypertension and mydriatic properties but that they reappear upon contact with tissues, particularly those rich in nerve terminations.—T. C. B.

Researches on ADRENALIN DIABETES. Achard (C.), Ribot (A.) & Binet (L.), *Lancet* (Lond.), 1921, ii, 139-140.

This is a brief but interesting report of experiments on the effects of adrenalin on carbohydrate metabolism. Series of experiments were performed on the influence of adrenalin on the glycolytic power of the organism, indicated by provoked hyperglycemia, on the relations between adrenalin and pancreatic extract, and on the effect of adrenalin on the depancreatized animal. Dogs were used as the experimental animals. For the first series of experiments, hyperglycemia was first provoked by intravenous injection of from 3.5 gms to 7.0 gms. glucose, and the blood glucose curve determined. With such curve as a control a similar amount of glucose was given in like manner on a subsequent date but with addition of 1 mg. of adrenalin. Adrenalin was also injected alone. It was found that more marked and more prolonged hyperglycemia was produced by adrenalin than by the small dose of sugar given and that it was greater when the two were injected together than the sum of both increases. It was concluded that the organism under the influence of adrenaline is unable to fix and burn sugar. Fresh pancreatic extract reduced hyperglycemia when injected, and when added to adrenalin inhibited the effects of the latter. In the third series of experiments the mechanism of adrenalin hyperglycemia was studied by repetition of the above experiments, but on depancreatized dogs. It was found that no hyperglycemia followed the injection of adrenalin in these animals. The conclusion is drawn, therefore, that the adrenalin exerts its action on carbohydrate metabolism only by inhibiting the glycolytic function of the pancreas.—I. M.

The action of atropine upon the effects of ADRENALIN on the uterus (L'action de l'atropine sur les effets provoqués par l'adrénaline sur l'utérus). The importance of atropine for the effects of ADRENALIN on the vessels and on the heart (Importance de l'atropine pour les effets de l'adrénaline sur les vaisseaux et sur le cœur). Action of atropine upon the effects provoked by ADRENALIN on blood pressure (Action de l'atropine sur les effets provoqués par l'adrénaline sur la pression du sang). Backman (E. L.) & Lundberg (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 475-483.

Employing the method of Magnus the action of atropine on various surviving organs has been examined. When adrenalin causes an augmentation of tonus and increased automatism, the addition of 10 mgm. of atropine sulphate to the bath will arrest the motor effects of the adrenalin. This action of atropine can be abolished by lavage, and the motor effects reappear. The uterus of the rabbit, guinea pig, cat, weasel and mouse was used. Atropine suppresses the action of adrenalin on isolated blood vessels. If we inject a cat with a large quantity of atropine, 2 cc. of adrenalin solution has no effect on the blood pressure, while the same quantity has a marked pressure effect before atropinisation. Atropine evidently paralyzes not only the parasympathetic, but also the motor part of the sympathetic. It does not act on the inhibitive side of the nervous system.—T. C. B.

(ADRENIN) The relation of blood supply and blood flow to sweating produced by pilocarpine. Burn (J. H.), *J. Physiol. (Lond.)*, 1922, **56**, 232-247.

The sweating response to pilocarpine depressed after complete denervation can be temporarily restored by subcutaneous injections of adrenaline or by a period of ether anesthesia. Degeneration of the sympathetic nerve supply is not followed by diminished pilocarpine response. It is possible that adrenaline delays the disappearance of capillary tone consequent on degeneration of the sensory fibers.—T. C. B.

(ADRENIN) Pseudo-paradoxical pupil-dilatation following lesions of the different paths. Byrne (J.), *Am. J. Physiol. (Balt.)*, 1922, **61**, 93-105.

Of endocrine interest in that adrenalin was used in the experiments.—T. C. B.

(ADRENIN: PITUITRIN) Studies on the physiology of the capillaries. V. The reactions of the human skin capillaries to drugs and other stimuli. Carrier (E. B.), *Am. J. Physiol. (Balt.)*, 1922, **61**, 528-547.

Of endocrine interest in that the constriction of the capillaries under influence of adrenalin and pituitrin has been directly observed in the human skin by Lombard's method.—T. C. B.

The vomiting of pregnancy with acidosis. The treatment with glucose and ADRENALIN. Therapeutic abortion. Cure (Vomissements incoercibles de la grossesse avec acidose. Echec du traitement hydrocarburé et de l'adrénaline. Avortement thérapeutique. Guérison). Cathala (V.) & Biancani (E.), Bull. d'obst. et gynéc. de Par., 1922, 11, 219-223.

Adrenalin and glucose treatment proved ineffective.—F. S. H.

A further report on the classification of birth paralyses as ENDOCRINES. Clarke (L. B.), South. M. J. (Birmingham), 1922, 15, 534-536.

Excluding cases of pure cretinism, unassociated, 30 cases of apparent birth paralysis have been under observation since February, 1919. One case report is given. The observations justify to the author the belief that many cases showing mental or physical deficiency or birth paralysis are due to disordered functions of the ductless glands.—F. S. H.

ADRENIN by intravenous injection. Cardio-vascular effect on the normal man (Épreuve de l'adrénaline en injection intraveineuse. Action cardio-vasculaire chez l'homme normal). Daniélopou (D.) & Carniol (A.), Ann. de méd. (Par.), 1922, 12, 127-149.

Amounts of adrenin ranging from 1:50,000 to 1:250,000 were injected into the subject in the reclining position and records made of the blood pressure. The tracings of the results are given. The conclusion is made that the drug is not a specific sympathetic stimulant, but induces reaction in the entire vegetative system. Because of the rapid destruction, intravenous administration is preferred to subcutaneous. The intravenous injection gives rise to 3 groups of phenomena: modification of cardiac rhythm; modification of arterial tension; and subjective disturbances. All occur when the strong dose of 1:100,000 is given. When weaker doses are administered, the cardio-vascular phenomena alone appear. There is first cardiac acceleration, then depression as the dose becomes smaller.—F. S. H.

Action of ADRENALIN on the human stomach, administered intravenously or by mouth (Action de l'adrénaline sur l'estomac de l'homme. Voie intraveineuse et voie gastrique). Daniélopou (D.) & Carniol (A.), Compt. rend. Soc. de biol. (Par.), 1922, 87, It was 718.

nal in movements of the stomach were recorded by the method of the adren modified. The intravenous injection of small doses of adrenin (1:100,000) produces an exaggeration of the gastric contrac-

tions. Large doses (1:100,000; 1:50,000) clearly inhibit contractions, sometimes followed by exaggeration. Introduction into the stomach of 1 mgm. of adrenalin causes intense gastric contractions. From these results adrenalin is contraindicated in cases of hemorrhage from ulcers of the stomach.—T. C. B.

Studies of the expression in ENDOCRINOLOGY (*Estudo da facies em endocrinologia*). Dias (A.), *Rev. dos Cursos de la Fac. de med. (Porto Alegre, Brazil)*, 1921, 7, 214-235.

A discussion of the value of the study of the facial expression in the diagnosis of disorders of the endocrine system. The paper has many photographs depicting the facies characteristic of the more typical disturbances. With the exception of one case of acromegaly all the illustrations have been taken from reports by other workers
—F. S. H.

The influence of ADRENALIN on nephritis and its complications by injection into the kidney. Eaton (G. D.), *Calif. State J. M. (San Fran.)*, 1921, 19, 233-237.

Laboratory animals injected with 0.5 cc., 1:500 dilution of venom from a rattlesnake which had previously received injections of adrenalin caused death in a few hours. When 0.5 cc. of adrenalin was given along with the venom there was but little toxic effect. The same amount of venom from a snake which had not previously received injections of adrenalin caused death in ten minutes. The above experiments led the author to attempt the use of adrenalin in the treatment of the toxemia of nephritis. One patient, in shock because of severe hematuria of the right kidney, which was later shown to be tuberculous, received 1 cc. of adrenalin solution injected into the pelvis of the kidney. The blood pressure, which before the injection was 80/0, arose to 120/70. In other patients with nephritis and high blood pressure the administration of adrenalin into the pelvis of the kidney was followed within 24 hours by a fall of the pressure and an increase in the output of urine. Case reports are given illustrating the effects of pelvic injections of adrenalin on various degrees of nephritis.—H. W.

(ADRENIN) Blood sugar studies. Foster (G. L.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 19, 408-412.

Results of the administration of various sugars to man and study of the blood sugar curves leads Foster to the belief that the epinephrine hyperglycemias are not to be reconciled with the hypotheses of Folin and Berglund (*J. Biol. Chem.*, 1917, 30, 79). The conclusion is drawn that the chief factor in preventing hyperglycemia is glycogen formation, since this is presumably the only carbohydrate function which is upset by epinephrine. The possibility of there being present a substance analagous to secretin is mentioned.
—F. S. H.

Action of ADRENIN on liver glycogen and on the weight and volume of the frog's liver (*Action de l'adrénaline sur le glycogène hépatique et sur le poids et le volume du foie chez la grenouille*). Gautier (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 157-159.

Adrenalin causes diminution or complete disappearance of glycogen from the liver of warm blooded animals. No experiments of a similar nature seem to have been made on cold blooded animals. This paper deals with the frog. Methods and protocols are given. From the results it is concluded that adrenalin injected several times diminishes the liver glycogen, but less intensely and less rapidly than in warm blooded animals.—T. C. B.

Circulation of ADRENIN in the frog after injection into the dorsal sac (*Circulation de l'adrénaline chez la grenouille après injection dans les sacs dorsaux*). Gautier (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 159-161.

If a frog is killed by section of the bulb, the eyes removed, and exposed to a strong light for half an hour, the pupils contract strongly. If the eye is then placed in water or saline solution, the pupil dilates. If the liquid contains adrenalin the dilatation is marked, and then a second exposure to bright light is not followed by myosis, or there is greater dilatation. If the doses of adrenalin is small, there may be slight constriction, but much less than the control in saline without adrenalin. If adrenalin is injected into the dorsal sack, strong dilatation occurs. If the animal is killed at the end of an hour, the enucleated eye exposed to artificial light does not respond by contraction of the pupil, but remains dilated. This resistance to the action of light may last 12 hours. Hence the tissues of the eye presumably remain impregnated with adrenalin. Blood from the abdominal vein of a frog injected with adrenalin 4 hours previously, causes mydriasis. After 20 minutes it is put in the blood from a second injected frog, and the dilatation becomes very marked. There is a cumulative action, permitting the absorption of more adrenalin. Three-quarters of an hour after injection of adrenalin into the leg, the enucleated eye is dilated. If the animal is killed and the eye exposed to light there is a partial contraction of the pupil, but the lumino-resistant mydriatic reaction is still present. This is considered evidence of the presence of adrenalin in the venous blood far from the zone of injection. As adrenalin cannot be discovered in the blood of mammals (Falta and Preistly), it must circulate in a combined state.—T. C. B.

The diverse effects of ADRENALIN upon the migration of the scale pigment and the retin. I pigment in the fish, *Fundulus heteroclitus*, Linn. Gilson (A. S.), *Proc. Nat. Acad. Sc. (Balt.)*, 1922, **8**, 130-133.

Report of experiments on fundulus which demonstrate that the injection of adrenalin will cause distal migration of the pigment processes in the retinas of animals that have been kept in the dark, but produces no significant change in the already extended processes of animals that have been exposed to the light. The changes in scale pigment is of a reverse nature.—T. C. B.

Studies in fatigue. XI. The effect of intravenous injection of massive doses of ADRENALIN upon skeletal muscle at rest and undergoing fatigue. Gruber (C. M.), *Am. J. Physiol. (Balt.)*, 1922, 61, 475-492.

In discussions upon the effect of adrenalin on skeletal muscle, its action on fatigued muscle has not been sufficiently considered, and this is one of the problems the author has set out to solve. The usual graphic methods were used on cats. Adrenalin injected intravenously has the same effect on non-fatigued and fatigued muscles. It lowers the threshold and increases the height of contraction as much as 240 per cent, if the dose is large. This increase depends on the concentration of adrenalin, the rate of stimulation and the condition of the animal. Slowly injected, the results are not so marked. The effects are only slightly, if at all, due to changes in pressure or bettered circulation. Adrenalin does not neutralize fatigue products, but increases the irritability of muscle, whether fatigued or not.—T. C. B.

Active and potential ADRENIN. In regard to the note by Abelous and Soula (*Adrénale active et adrénaline virtuelle. A propos de la note de MM. Abelous et Soula*). Nicolas (E.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 849-850.

An objection to the work of Abelous and Soula on the ground that the horse serum used is a formalized serum, and a suggestion that the experiments be repeated with a serum free from such objections.—T. C. B.

ADRENALIN and liver glycogen (Adrénaline et glycogène du foie). Doyon (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 598.

Richter, in an article on the relation which exists between fever and the elimination of sugar, alluded in a few words to the action of adrenalin on the liver glycogen. Doyon was the first to demonstrate that adrenalin causes glycogen to disappear from the liver of the dog and rabbit. His results were extended to the frog by Gautier.

—T. C. B.

Action of ADRENALIN on the striated muscular system (Action de l'adrénaline sur le système musculaire strié). Guglielmette (J.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 692-694.

Resumé of experiments which lead to the conclusion that adrenalin modifies the contraction, excitability and latent period of fatigued muscles by acting on the neuro-muscular junction.—T. C. B.

The liberation of EPINEPHRIN during muscular exercise. Hartman (F. A.), Waite (R. H.) & McCordock (H. A.), *Am. J. Physiol.* (Balt.), 1922, **62**, 225-241.

A continuation of experiments previously described, in which proof is given that dilatation of the denervated pupil during exercise is due to epinephrin. The maximum output reached depends upon the intensity and duration of the exercise. There is an after secretion which lasts for a varying length of time, according to the vigor and duration of the exercise.—T. C. B.

(ADRENIN) The reaction to EPINEPHRIN administered by rectum. Hoskins (R. G.), *J. Pharmacol. & Exper. Therap.* (Balt.), 1921, **18**, 207-211.

Dogs and cats were used. Blood pressure and peristalsis were recorded. Doses of 1 to 5 mgm. of epinephrin produced either no or relatively slight effects.—J. B. C.

The rôle of ADRENALIN in the hypertensive effects produced by excitation of the splanchnics or by bulbar puncture (*Rôle de l'adrénalin dans les effets hypertensifs produit par excitation du nerf splanchnique ou par piqûre bulbaire*). Houssay (B. A.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 695-698.

Confirmation of the results of Tournade and Chabrol that stimulation of the splanchnics causes a direct vaso-constriction and also a constriction due to adrenalin liberated from the adrenals.—T. C. B.

Comparative studies on respiration. XXIII. The effect of ADRENALIN on the production of carbon dioxide by animals and by plants. Hutchinson (D. M.), *Am. J. Physiol.* (Balt.), 1922, **62**, 192-196.

The effect of adrenalin on the production of CO₂ by radish seedlings and by frog's muscle is similar. Stronger solutions (0.002-0.003 per cent) cause a depression, followed by a return to normal; weaker solutions produce a rhythmic effect; the CO₂ falls, rises, falls and rises again.—T. C. B.

Some modifications of the colorimetric method for the determination of ADRENALIN by Folin, Cannon and Denis. Kodama (S.), *J. Biochem.* (Tokyo), 1922, **1**, 281-287.

A new standard color solution is used, made as follows: Grüber's Water blue (0.1g. per liter) 4 cc.; Grüber's Nigrosin (0.1g. per liter) 4 cc.; CuSO₄ · 5H₂O (10%) 10 cc.; HCl (sp. gr. 1.05) 10 cc., and H₂O to 100 cc. The above mixture when set at 20.6 in a

Dubosq colorimeter corresponds to the color developed with 0.1 mg. of adrenalin set at 20.0 mm. The uric acid reagent of Benedict and Hitchcock (J. Biol. Chem., 1915, 20, 619) and 20% Na_2CO_3 are used for the development of the color in the test solution.—F. S. H.

The influence of **ADRENALIN** on the permeability of the muscle bundle membrane (*Die Einwirkung des Adrenalins auf die Permeabilität von Muskelfaschengrenzschichten*). Lange (H.), *Ztschr. f. physiol. Chem.* (Strassb.), 1922, 120, 249-236.

Adrenalin has the ability to increase the permeability of the limiting membrane of striated muscle of the frog.—F. S. H.

The secretion of sweat. Part II. The effect of vaso-constriction and of **ADRENALIN**. Langley (J. N.) & Uyeno (K.), *J. Physiol.* (Lond.), 1922, 56, 206-226.

A continuation of the work previously reported (see *Endocrin.*, 1922, 6, 529). The secretory effect of adrenaline was generally less than that of Ringer's solution, whether it was used in 0.001 per cent or 0.1 per cent solution. The secretion is limited to the area injected. These facts lead to the conclusion that it is the fluid and not the adrenaline that causes the secretion, and it is less because of the decreased blood supply to the glands, which in turn causes a lowering of skin temperature. Pituitrin produces insufficient vaso-constriction to interfere with secretory activity.—T. C. B.

(**ADRENIN**) Remarks relative to the communication of M. Dorlencourt. Netter (A.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1131.

Opinions differ as to the absorption of adrenalin by the digestive tract. Ingestion has no effect on blood pressure; on the other hand, clinicians obtain beneficial results. The authors have shown that chlorolose has a stabilizing effect on the amount of blood sugar, and have used this method to solve the problem. A dog was anesthetized with chlorolose and the normal glycemia determined at 15 minute intervals. Then 8 cc. of a solution of adrenalin, 1:1000, in 40 cc. of water was introduced by stomach tube and blood sugar determinations made every 10 minutes. The hyperglycemia which followed was very marked and progressive, reaching a maximum in about 50 minutes. There can be no doubt, then, that adrenalin is absorbed by the digestive tract [see Absorption of adrenin by the digestive tract (*Absorption de l'adrénaline par voie digestive*). Dorlencourt (H.), Trias (A.) & Paychère), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1129-1131].—T. C. B.

Treatment of rachitis with **ADRENIN** (*Behandlung der Rachitis mit adrenalin*). Lenert & Weinberg, *Munchen med. Wchnschr.*, 1921, 68, 1482-1484.

Adrenin hydrochloride 1:1000 was administered 3 to 4 times daily in doses of 0.2, increasing to 0.5. In addition calcium carbonate was given three times daily in small amounts (what would be contained on a knife-tip) for 4 to 6 weeks. This treatment is indicated in all severe cases of rachitis where the usual anti-rachitic treatment is unavailing.—F. S. H.

EPINEPHRIN hypersensitiveness and its relation to hyperthyroidism.

Peabody (F. W.) & Sturgis (C. C.), Tr. Ass. Am. Physicians (Phila.), 1920, 35, 110-121.

See Endocrinology, 1922, 6, 128.

ADRENALIN in the Stokes-Adams syndrome. Phear (A. G.) & Parkinson (J.), Lancet (Lond.), 1922, 1, 933-936.

This paper gives a detailed description of a case of heart block in a woman of 49 years with frequent fainting spells. Prompt relief from the attacks and increase in ventricular rate followed the subcutaneous injection of .5 minims of 1:1000 adrenalin. After the repetition of the injection, but with a 10 minim dose, the patient remained free from attacks throughout the remainder of her stay in the hospital (4 weeks). The authors did not feel certain as to complete disappearance of the block, although they assumed that mechanism had probably returned to normal. Literature on the is briefly discussed.—I. M.

ADRENALIN hyperglycemia and hyperglycorachia (Hyperglycémie et hyperglycorachie adrénaliques). Polonovski (M.), Duhot (E.) & Morel, Compt. rend. Soc. de biol. (Par.), 1922, 87, 679-680.

Experimental adrenalin hyperglycemia is always connected with a hyperglucorachia, the sugar in the spinal fluid appearing a little more slowly, and slightly inferior in quantity to that in the blood. Observations on glycorachia, therefore, should be reported in relation to the hyperglycemia present in a given case.—T. C. B. 192-196.

The effect of the vomiting of pregnancy (L'adrénaline dans les vomissements et les nausées incoercibles de la grossesse). Rathery (F.), Bull. 0.003 per cent) J. de Par., 1922, 11, 215-219.

weaker solutions and that the administration of 1 mg. of adrenalin in and rises again.—logical serum subcutaneously, or from 1 to 2 mg.

Some modifications of uncontrollable vomiting of pregnancy gave good results. Number of cases.—F. S. H.

of ADRENALIN Biochem. (Tokyo), 1922, 1, 100-101.

A new standard method of the physiological control method for Grubler's Water blue (0.

(0.1g. per liter) 4 cc.; CuSO₄ solutions each of 0.03 mg. of adrenaline into 10 cc., and H₂O to 100 cc. at intervals, gave, respectively, 7.7, 9.2

and 9.9 cm. instead of equal increase of pressure (cf. Chem. Abst., 16, 2385). The habitual average error in Cushny's method varies between 20% and 30%. Still, this method of determining adrenaline content will remain very valuable in the hands of the experienced.

—Chem. Abst., 16, 2574.

ENDOCRINE GLANDS in gynecology (*Glandulas de secreção interna em gynecologia*). Rosa (O.), Rev. dos Cursos de la Fac. de med. (Porto Alegre, Brazil), 1921, 7, 82-91.

No new data.—F. S. H.

The action of **ADRENIN** upon guinea pigs (*Untersuchungen über die tödliche Adrenalinwirkung am Meerschweinchen*). Schmidt (L.), Ztschr. f. d. ges. exper. Med. (Berl.), 1919, 9, 285-307; abst. Zentralbl. f. Biochem. u. Biophysik, 1920, 22, 111.

A subcutaneous dose of 0.8 mg. per kg. of adrenin is fatal; an intravenous dose of 0.08 to 0.15 mg. per kg. causes multiple pulmonary hemorrhages and death. Previous administration of a sublethal dose within the preceding 24 hours lowers the fatal dose and leads also to pulmonary hemorrhages, repetition of which causes death.—R. G. H.

Vascular reaction to EPINEPHRIN in perfusates of various Ch. II.

The portal-venous system of the liver. Snyder (C. D.) & Martin (L. E.), Am. J. Physiol. (Balt.), 1922, 62, 185-191.

Perfusing the turtle's liver with Ringer's solution of varying H-ion concentration "shows conclusively that, with the H-ion concentration of a perfusing fluid set somewhat above that of the vascular blood of animals, epinephrin when given in minimal effective dosage is an inhibiting or a depressor agent. With the H-ion concentration set somewhat below that of the blood of the general circulation epinephrin given in the same minimal dosage still has the exciting or pressor action that is observed invariably for larger doses." The relation of these facts to the effect of epinephrin on the general blood pressure is discussed.—T. C. B.

Infantile tolerance to ADRENIN (*Tolerancia infantil a la suprarenina*). Soler (B.), Arch. españ. de pediat. (Madrid), 1922, 6, 146-150.

The author describes a girl of 4½ years who had received 12-15 drops of adrenin thrice daily for 26 months without any ill effect. The drug had been given the father of the patient because of Addison's disease. Soler reviewed the therapeutic effects of adrenal preparations, but found no activity following the oral administration in this child.—C. H. G.

(ADRENIN) The action of vaso-constrictor substances on the blood vessels and pigment cells of the frog's web. II. Stepanov (G. T.),

J. russe de physiol., 1919, 2, 103-115; abst., *Physiol. Abst.*, 1920, 5, 487.

Adrenalin constricts the blood vessels and evokes or increases their spontaneous periodic contractions. The action of adrenalin does not depend on the central nervous system. The pigment cells contract when adrenalin or Ca salts are administered. Pituitrin does not contract the cells. These drugs were injected subcutaneously.—*Chem. Abst.*, 15, 2672.

The function of the sympathetic nerve supplying the intestine and the action of ADRENALINE. Tashiro (K.), *Tohoku J. Exper. Med. (Sendai)*, 1922, 1, 102-105.

Using cat's intestinal strips Tashiro obtained responses after the application of adrenaline which led him to the conclusion that in the sympathetic nerve supplying the intestine there exist, besides the inhibitory nerve fibers, fibers which convey augmentatory impulses, and that the circular muscle is supplied by the latter and the longitudinal muscle by both inhibitory and augmentatory fibers. Adrenine stimulates these nerve endings and whether it excites or inhibits depends upon its quantity.—F. S. H.

The paradoxical action of ADRENALINE on the pupil of the eye in animals after repeated treatment with that drug. Kato (T.) & Watanabe (M.), *Tohoku J. Exper. Med. (Sendai)*, 1920, 1, 73-82.

In cats which were previously treated with daily excessive hypodermic injections of adrenin for some weeks, the administration of a minute amount of the drug into the carotid gave rise to a constriction of the pupil. Intravenous injections gave no such effect. In the pupil of such treated animals constriction is usually observed after the instillation of adrenin. The paradoxical action of the drug on the pupil occurs only rarely in animals previously not treated with repeated administrations of adrenin. When the previous treatment has been by instillations instead of injections the further instillation of minute amounts is always followed by miosis lasting for 5 to 8 hours. The instillation of cocaine or pituitrin in the previously treated eye and of phystostigmine produce effects less marked on the treated side than the non-treated. The paradoxical action is probably based on the altered chemism of the dilator muscles of the pupil.—F. S. H.

Vertigo and its treatment through ADRENALIN. Vernet (M.), *Laryngoscope (St. Louis)*, 1922, 32, 205-213.

The author uses adrenalin, 1 to 1000 solution, in doses of from 5 to 20 drops twice a day for the control of vertigo.—H. W.

Action of atrophine on the effects exercised by ADRENALIN upon blood vessels (*Action de l'atropine sur les effets exercés par*

l'adrénaline sur les vaisseaux sanguins). Wehland (N.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 774-776.

Perfusion experiments on the frog, by which it is again shown that atropin paralyzes the motor part of the sympathetic, and causes an inversion of the effects of adrenalin on the blood vessels.

—T. C. B.

Clinical observations on treatment and progress in **DIABETES**.

Allen (F. M.) & Sherrill (J. W.), *J. Metab. Research (Morristown)*, 1922, **1**, 377-434.

The authors call attention to the value of publishing full and frank statements of the results of treatment in diabetes and summarize in some detail their own findings over a number of years. They discuss also the results of treatment as followed by various other workers, especially those of Petré and Newburg and Marsh. The principle of under-nutrition in the treatment of diabetes is strongly defended and it is pointed out from Allen's observations on his Rockefeller Institute Hospital series, followed since 1914, that mortality was much higher in cases with complications. Tuberculosis, the most serious of the complications, increases the hopelessness of the prognosis greatly in the young, but may often be kept under control in older patients when the diabetes is under control. The authors believe that sodium bicarbonate may be of benefit in combating acidosis if not used to extreme, and if employed only as an accessory to the methods employed for preventing the development of acids. The authors' method of treatment in diabetes consists of two phases. In the preliminary phase, the patient is put on a very low diet, consisting chiefly of proteins to which a small portion of carbohydrate is added in cases with acidosis and bulky materials without food value if the bowels need stimulating. The patient is kept on this diet until the blood sugar is normal, after which the diet is gradually increased, with blood sugar determinations as a guide, until the final diet is reached, which approaches as nearly as possible a maintenance diet for the particular patient under treatment. The principle underlying the treatment is functional rest to assist in conservation and regeneration of function. The work of Petré and Newburg and Marsh, who sponsor high fat diets in the treatment of diabetes, is criticized adversely by the authors on the basis of their exceeding the total metabolic tolerance of the patient and aiding in the development of acidosis. Although dietary therapy, which preserves the normal blood sugar level, appears in many cases to check the progress of diabetes, the authors agree that it is too early to say finally that there is not a "spontaneous downward" course in this disease in spite of treatment.—I. M.

Experimental researches on **DIABETES insipidus** and **dystrophia adiposogenitalis** (*Recherches expérimentales sur le diabète in-*

siptide et le syndrome adiposogénital). Bailey (P.) & Bremer (F.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 925-927.

Camus and Roussy have shown that diabetes insipidus is due to lesion of the para-infundibular region and not to lesion of the hypophysis. The lesions were made by the buccal route. The authors have repeated the experiments using the temporal route of Paulesco and of Cushing. Even a minute lesion of the para-infundibular region of the hypothalamus provokes polyuria in dogs; it is transitory or permanent according to the extent of the lesion. If permanent, cachexia, genital atrophy and adiposity result. Permanent polyuria has all the characteristics of diabetes insipidus in man. Polyuria occurs after denervation of the kidneys, thus excluding vasomotor disturbances. Protocols of two experiments are given, with histological findings and location of the lesion. The meninges and the hypophysis were normal, and nothing indicated that the hypophysis was concerned.—T. C. B.

Pancreatic extracts in treatment of DIABETES MELLITUS. Banting (F. C.), Best (C. H.), Collip (J. B.), Campbell (W. R.) & Fletcher (A. A.), *Canad. M. Ass. J.*, 1922, 12, 141-146.

Believing that the active principle of the pancreas is destroyed by the digestive enzymes in the ordinary extracts of the gland, an extract was made with ice-cold Ringer's solution from degenerated pancreatic tissue removed ten weeks after the ducts were tied. Such extract, injected intravenously and subcutaneously into a diabetic dog, caused marked reduction in blood sugar and in the sugar in the urine. A completely diabetic animal was kept alive 70 days and then chloroformed. Control extracts of liver and spleen did not produce any effects. Later, one of these workers prepared an extract of the whole gland which was sterile, highly potent and could be injected subcutaneously in the human subject. Seven clinical cases are referred to which showed marked clinical improvement as well as reduction in the blood sugar and a rise in the respiratory quotient. A later report will be made on the method of making the extract.

—J. H.

The effect of PANCREATIC extract (insulin) on normal rabbits.

Banting (F. G.), Best (C. H.), Collip (J. B.), Macleod (J. J. R.) & Noble (E. C.), *Am. J. Physiol. (Balt.)*, 1922, 62, 162-176.

Insulin injected subcutaneously into normal rabbits causes the percentage of blood sugar to fall within a few hours. As a tentative basis for the physiological assay of insulin the authors consider as one unit the number of cubic centimeters which causes the blood sugar of normal rabbits to fall to 0.045% within 4 hours. This dose is decidedly active in lowering the blood sugar in diabetic patients. As the blood sugar falls the animals exhibit characteristic symptoms of hunger and thirst, hyperexcitability and fear. The animals may

recover but frequently have, with active preparations, clonic convulsions lasting several minutes, and the blood sugar is found to be about 0.045%. If they die there is a peculiar mucilaginous degeneration of the subcutaneous tissues of the abdominal wall. Injections of solutions of dextrose subcutaneously antidote the insulin and the rabbit is normal in a few minutes.—T. C. B.

(DIABETES) An improved alimentary glucose tolerance test. Beeler (C.), Bryan (A. W.), Cathcart (E. P.) & Fitz (R.), J. Metab. Research (Morristown), 1922, 1, 550-560.

The authors undertook the task of improving the usual alimentary glucose tolerance test. Since atypical blood sugar curves indicating diminished tolerance have been reported in diabetes, diseases of the liver, obesity, nephritis, hyperthyroidism, cancer, rickets, arthritis, etc., the test has become very popular and doubtless has much value if properly controlled. Woodyatt, Sansum and Wilder, using the intravenous method, have pointed out that in some diseases what appears to be an increased tolerance or a delay in the rise of the blood sugar curve may be due merely to poor alimentary absorption. The present authors have, therefore, made a brief study of the factors of importance in absorption and apply these in their modification of the alimentary test. Both normal and diabetic subjects were given sugar in varying concentrations after gastric aspiration and then the stomach contents were aspirated one hour later to determine the amounts of sugar unabsorbed and the concentration of the remaining solutions. Hemaglobin and blood sugar determinations were made at the same time at intervals. It was found that absorption of the sugar was most rapid when the concentration of the solution given was between 10 and 20 per cent. Concentrated solutions were found to delay absorption and to draw fluid into the stomach from the blood stream, the hemaglobin of the blood increasing, due to the loss of this fluid. The suggested modification of the alimentary glucose tolerance test based on these findings and those of Woodyatt, Sansum and Wilder is as follows. A fasting subject is given 500 cc. of a 20 per cent glucose solution. One hour later the stomach is completely emptied and the amount of sugar contained is estimated. This subtracted from the quantity administered gives the amount absorbed in one hour. Blood sugar and hemaglobin determinations, which are made before glucose ingestion at the time the stomach is emptied and at later intervals, are employed for calculation of changes in blood volume. The results are made uniform by estimating from these data the proportional blood glucose values which would have been obtained under the same conditions outlined had 0.800 gm. of glucose per kg. per hour been given, the maximum dose found to be tolerated without producing glycosuria. Diabetics gave a typical curve in all instances.—I. M.

Effect on DIABETICS of lumbar puncture. Bickel (G.), *Rev. méd. de la Suisse Rom.* (Genève), 1922, 42, 231-233.

Bickel reports a drop in the sugar in the urine after lumbar puncture from 83 to 38 gm. per thousand in a diabetic woman of 73. The sugar content of the blood, fasting, also dropped from 3.39 to 2.25 per thousand. Lhermitte recently reported an analogous observation. His patient was a man of 76, and the glucose in the urine dropped temporarily after lumbar puncture from 28.45 gm. to 0.72 gm., while the output of urine was only 1 liter instead of the preceding 2.5 liters.—*J. Am. M. Ass.*, 79, 1084.

The etiology of DIABETES, and its bearing on treatment. Cammidge (P. J.), *Practitioner* (Lond.), 1922, 108, 396-402.

The author admits that the Allen fasting treatment is a distinct advance in the treatment of diabetes, but contends that some patients do not progress well under this method; rapidly increasing acidosis, nervous disturbances and ataxia sometimes result. Cammidge comes to the conclusion that not all cases of diabetes are due to pancreatic disease primarily, but that a fairly large group depends upon hepatic insufficiency and that this latter group does not respond well to the Allen treatment. He arrives at the differentiation by determinations of the difference between the percentage of sugar and total carbohydrate in a series of blood specimens taken at hourly intervals before and after a test breakfast. This he terms the "difference value" of the blood. The difference value curve and blood sugar curve are opposed in the typical pancreatic type, the former falling while the latter rises. Of 140 cases examined by this method 32 per cent gave this opposed pancreatic curve. Thirty-four per cent gave another type of curve which Cammidge reproduced in animals by interfering with liver function. Twenty-four per cent belonged in another group, showing a still different curve relationship, the cause of which he has not yet determined.—*H. L.*

The retinas of Bright's disease in DIABETES (*Les rétinites brightiques des diabétiques*). Cantonnet (A.), *Progrès méd.* (Par.), 1919, 34, 468-469.

Presentation of cases of diabetes in which the retinitis was not of diabetic origin, but was probably nephritic since the urine contained protein, and the blood urea and pressure were high. The conclusion is drawn that all cases of retinitis in diabetes are not of diabetic origin.—*F. S. H.*

Massive doses of alkali in two cases of impending DIABETIC coma. Cary (W. E.), *J. Am. M. Ass.* (Chicago), 1921, 76, 1393-1395.

In view of the much debated question of the use of alkalis in diabetic acidosis, Cary reports two cases in which massive doses of sodium bicarbonate caused definite subjective and objective im-

provement. The alkalis should be given by mouth when possible. In the first case, a man of 23 received 350 grams of sodium bicarbonate in 72 hours, with striking improvement subjectively and with a return of pulse and respiration to normal. The other patient, a boy of 15, received 240 grams in 43 hours with similar improvement. Both patients were on absolute fast during the period of this therapy. The carbon dioxide combining power of the plasma rose from 13.63 to 64.61, and from 14.31 to 45.83 per cent by volume, respectively, in the two cases. Cary concludes that the administration of sufficient alkali is beneficial, but warns against overalkalinization, which can be guarded against by examination of the urine or blood.—W. M. A.

Pleuro-pulmonary granulation clinically simulating typho-bacillosis in a **DIABETIC** (*Granulie pleuro-pulmonaire a allure clinique de typho-bacillose, chez un diabétique*). Caussade (G.) & Doumer (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1921, 45, 942-949.

A case report not of endocrine interest.—F. S. H.

Mode of action of carbohydrate-free diets in cases of **DIABETES** (*Du mode d'action des régimes anhydrocarbonés chez les diabétiques*). Chabanier (H.), Lebert (M.) & Lobo-Onell (C.), Compt. rend. Soc. de biol. (Par.), 1921, 85, 2-4.

Observations on 10 diabetics, 5 lean and 5 fat, especially in regard to the critical glycemia and the secretion threshold for sugar. The severity of the diabetes is indicated by the amount of blood sugar necessary to prevent acetonuria. Unless the acetonuria disappears there is no improvement.—T. C. B.

Report of two **DIABETIC** cases in the young. Davis (R. H.), Kentucky M. J. (Bowling Green), 1922, 20, 576-577.

Rigorous treatment of diabetes in the young is productive of good results.—H. W.

Stabilization of the amount of **GLYCEMIA** in the dog during chloralose sleep (*Stabilisation du taux de la glycémie chez le chien durant le sommeil chloralosique*). Dorlencourt (H.) & Psychère (A.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1078-1080.

During general anesthesia by chloralose the blood sugar equilibrium is relatively stable.—T. C. B.

The diet in **DIABETES** (*Le régime alimentaire des diabétiques*). Dumont (J.), Bull. Acad. de méd. (Par.), 1922, 87, 721-724.

Dumont expatiates on the great advantage in diabetes of giving carbohydrates that generate levulose rather than glucose. Ever since 1915 he has thus guided the diet in about twenty cases annually, and gives the details of one typical case. With a weight

of 100 kg. the man averaged from 200 to 250 gm. of glucose daily in about 2,500 to 2,800 cc. of urine. Milk was dropped and bread reduced to 200 gm., and the glucose output declined to 135 gm. and to 106 gm. when boiled potatoes were given instead of bread. Then vegetables producing inulin (jerusalem artichokes, salsify and scorzonera or viper's grass) were taken to a total of 150 gm. at a meal, and the glucose increased only to 10.8 gm. on the ordinary diet. Then for three months the artichokes were resumed, and the glucose disappeared almost completely. As the end of the year approached, the urine averaged only 2.5 gm. of glucose. In another case the output was 200 gm. of glucose and there was a carbuncle on the head. The man was cured in a few weeks and the glycosuria disappeared after the carbohydrates were given in the form of artichokes. He says, "This valuable plant reeducates the intestine by the levulose it brings and the modification of the intestinal flora. Foods producing inulin and levulose seem to reenforce the defensive forces of the diabetic while supplying the elements necessary for energy and heat."—J. Am. M. Ass., 79, 1000.

The dietetic treatment of surgical DIABETES. Ezell (J. J.), Kentucky M. J. (Bowling Green), 1922, 20, 421-423.

In the presence of infections "operate first and starve and diet afterwards." In operations of choice best results are obtained by first making the patient sugar free.—H. W.

Artificial pneumothorax for pulmonary tuberculosis with coexisting DIABETES of unusual onset: report of case. Geer (E. K.), Am. Rev. Tuberculosis (Balt.), 1922, 6, 399-401.

Geer reports two cases of pulmonary tuberculosis with co-existent diabetes in which pneumothorax induced with no untoward effects which could be ascribed to the diabetes. The thoracentesis wounds healed promptly after each refill. In one of the cases the diabetes manifested itself several months after the onset of the pulmonary lesion.—J. Am. M. Ass., 79, 917.

Some observations and remarks on the Allen treatment of DIABETES MELLITUS. Hall (J. W.), N. Zealand M. J. (Wellington), 1921, 20, 122-146.

Reference verified from Index Medicus.

Effect of insulin (PANCREATIC extract) on the sugar consumption of the isolated surviving rabbit heart. Hepburn (J.) & Latchford (J. K.), Am. J. Physiol. (Balt.), 1922, 62, 177-184.

The average sugar consumption of the isolated rabbit heart perfused with Locke's solution was found to be 0.87 mgm. per gram per hour. When insulin of proved potency, as tested by its ability to lower the blood sugar in normal rabbits, was added to the per-

fusion fluid, the average sugar consumption rose to 3.06 mgm. per gram per hour. The average glycogen content of the treated and untreated hearts was practically the same.—T. C. B.

Widely distributed epithelial-xanthomata accompanying high-grade **DIABETIC** lipemia (Ueber weit verbreitete Haut-xanthomatose bei hochgradiger diabetischer lipaemia). Hoffman (E.), Deutsche med. Wchnschr. (Berl.), 1918, 44, 1050-1052.

Differential diagnosis of benign glycosuria and of **DIABETIC** sugar by the aid of intravenous injections of glucose (Diagnostic différentiel des glycosuries bénignes et du diabète sucré, à l'aide d'injections intraveineuses de glucose). Joergensen (S.) & Plum (T.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 455-458.

Not of immediate endocrine interest.—T. C. B.

A trial of eucalyptus infusion in **DIABETES**. John (H. J.), J. Metab. Research (Morristown), 1922, 1, 489-495.

Beneficial effects of eucalyptus infusions on diabetes have been claimed by a number of writers. The author reports the results of an attempt to test the validity of these claims under properly controlled conditions. Infusions of eucalyptus globulus obtained from southern California were given in large quantities over a long period of time to 20 diabetic patients, some with and some without the disease under control. The results were uniformly negative.—I. M.

(**DIABETES**) Glucose tolerance and its value in diagnosis. John (H. J.), J. Metab. Research (Morristown), 1922, 1, 497-548.

The author briefly reviews the literature as to the clinical use of the glucose tolerance test and points out the important conditions in which abnormal curves have been reported. The special purpose of this communication was to show, judging from his experience with the method on 100 cases, the significant factors in the test, such as the height of the blood glucose curve, the possibility of delay in absorption in the intestine, the effect of nausea, the relation of water intake, previous fasting, etc., to the curve and the methods used for determining the blood sugar. Subjects vary considerably in their response to the test and the author placed the cases studied in 4 groups according to gradations of assimilation as follows: (1) strong normal, (2) normal, (3) weak normal or pre-diabetic, and (4) diabetic. Renal threshold is not a fixed value for all normal persons. Nausea produces a temporary lack of absorption from the stomach which is characterized by a dip in the curve. Restriction of carbohydrates improves the tolerance in diabetics and in pre-diabetics as seen from repeated blood glucose curves. The author concludes that the sugar tolerance test is very useful in revealing an important number of cases of early or latent diabetes at the stage most susceptible to treatment.—I. M.

The laboratory as an aid in the treatment of DIABETES. Jonas (L.), Penn. M. J. (Harrisburg), 1918-1919, 22, 718-721.

Clinical determination of blood sugar and acidosis as guides in the management of DIABETES MELLITUS. Jonas (L.), Med. Clin. N. Am. (Phila.), 1918, 2, 861-869.

The metabolism of DIABETES. Joslin (E. P.), Tr. Ass. Am. Physicians (Phila.), 1920, 35, 85-87.

The total metabolism in diabetes is a varying factor, and, generally speaking, any definite statement in this regard has been avoided. However, it may be affirmed with reasonable certainty that the average metabolism of the diabetics studied in this country was increased prior to June, 1914 (the date of fasting experiments conducted by the author), and correspondingly decreased since that date. To a large extent these facts are explained by the severer cases in each group being those which were rigorously either over- or under-fed. If metabolism is above normal, there is a general tendency for it to rise with increasing acidosis. This relation does not hold in instances in which metabolism is decreased. It is possible that the extreme degree of undernutrition which was in process of development obscured the effect of the acidosis. The lower the respiratory quotient the higher the metabolism tends to rise. Other observations along these lines are in the making. The effect of the administration of levulose has been studied in 50 experiments on diabetes. The average of these experiments showed an increase of 17% in the metabolism. The more levulose given per kg. body weight, the greater the increase in the metabolism. Observations upon the metabolism in relation to the blood-sugar, blood-fat and non-protein nitrogen were also made. A distinct relation between the pulse and the metabolism was usually found. Besides the 50 experiments with levulose there were some 100 other food experiments. These data are to appear in a subsequent publication.—I. B.

Practical lessons for physicians and patients in DIABETES. Joslin (E. P.), Med. Clin. N. Am. (Phila.), 1921, 4, 1723-1732.

This article contains many practical points on the pliability of the diet in diabetes as well as in health, the danger of fat to the diabetic, the critical period of hypoglycemia in undernutrition, and renal glycosuria. "Pliability of the diet" is a term peculiarly applicable to diabetes, because of the possibility of extreme variations from the normal of the proportion of carbohydrate, proteid, and fat that may be administered with benefit. Early cases will become sugar free with certain restrictions, but it is to the credit of F. M. Allen that undernutrition was shown to be the basic principle underlying restrictive methods in diet. Success is obtainable only through continuous prolonged observation of the patient and avoidance of

fads. The dietary treatment of diabetes may be divided into two epochs, that preceding and that beginning with June, 1914, the date when the method of undernutrition was introduced. Joslin states that the two epochs of treatment differ so widely that if methods employed prior to June, 1914, were adopted now, it would almost seem like malpractice, while, were the present method of undernutrition employed prior to this date, it would have seemed like an unjustifiable experiment. Obesity exists with the onset of diabetes in 75% of cases, and in some decades of life in 39 cases out of 40. Recognition of obesity as an etiological factor should lead to a reduction in the number of diabetics through prophylactic undernutrition. The old-fashioned method of restricting the carbohydrates and increasing the fat and protein in the diet frequently led to death of the patient in diabetic coma within a few days. When the total caloric value of the diet is low, a comparatively high proportion of fat often appears to be harmless; but when the diet is fairly liberal and the proportion of carbohydrate to fat falls below 1 to 5, harm almost invariably results. The discovery of the presence of hypoglycemia during the course of treatment by undernutrition is an important danger signal. The author cites cases emphasizing this fact. The subject of renal glycosuria has received much attention in recent years. A case in a man of 39 is cited, in which there was a large percentage of sugar in the urine during a period of 27 years. At present the blood sugar is normal under all conditions, and the patient appears to be in good health. The teeth, circulatory system, kidneys and eyes are normal. In concluding his remarks on this patient, Joslin says, "A case like the present encourages one to hope that renal glycosuria may yet be proved to be an entity."—I. B.

The feeding of non-ketogenic odd-carbon fats to DIABETIC patients.

Kahn (M.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 265-266.

A synthetic fat as given in the title was fed to typical diabetic and ketotic patients. It was found that the fat was absorbed, that large amounts of it could be fed to these patients without inducing acidosis, and that the nutrition of such patients was improved.

—F. S. H.

The elimination of organic acids in the urine of DIABETIC acidosis

(L' élimination des acides organiques dans l'urine des diabétiques acidotiques). Labbé (M.), Bith (H.) & Nepveux (F.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 446-447.

Not of immediate endocrine interest.—T. C. B.

A study in experimental DIABETES. The effect of intravenous injection of pancreatic perfusates on the D/N ratio following pan-

createctomy. Landes (H. E.), Garrison (L. E.) & Moorhead (J. J.), Arch. Int. Med. (Chicago), 1922, 29, 853-866.

The D/N ratio was taken as a criterion for the carbohydrate consuming power of the animal. Dogs were depancreatized and the D/N ratios were determined daily. When these figures became rather constant for each animal, it was the plan to inject intravenously a quantity of fine dextrose dissolved in Tyrode's solution. Subsequent determinations of the D/N ratio should show the amount of dextrose retained after such injections. It was then proposed to perfuse the pancreas of a normal animal with Tyrode's solution containing dextrose, and to inject this perfusate intravenously, at the same rate, into an experimentally diabetic animal, with the expectation that the subsequent D/N ratios would show some change in dextrose utilization. This experiment was attempted on 15 dogs, but no conclusions could be drawn from the fluctuating figures. It was then decided to attempt to influence the onset and course of experimental diabetes by the intravenous injection of pancreatic perfusates alone. Twenty-seven dogs were used. Dogs injected immediately following pancreatectomy with 150 cc. of perfusate showed no delay in the onset of glycosuria, after which subsequent injections of perfusates produced no consistent change in the D/N ratio. Defibrinated blood drawn from pancreatectomized animals and passed once through the normal pancreas had no effect on experimental diabetes.—H. L.

Treatment of DIABETES and tuberculosis. Landis (H. R. M.) & Funk (E. H.), Am. Rev. Tubercul. (Balt.), 1922, 6, 429-437.

Landis and Funk believe that these two diseases are more commonly associated than is generally considered, and that in practically all cases diabetes is the initial disorder and the active tuberculosis a subsequent development. The diabetes probably determines in most instances the development of tuberculosis in the person in whom both are found to be present. The authors are quite convinced that in that particular group of tuberculous patients in whom diabetes is present, weight increases have less significance, as far as the improvement of the tuberculous condition is concerned, than in others, and this is in keeping with knowledge of the prognosis of diabetes. The undernourished diabetic keeps well longer than one who tends rapidly to put on weight. The tuberculosis will improve even though there is no considerable gain in weight, if the diabetes remains under control at a given weight. The important point in regard to the fats is to know how to adjust the diet so that a maximum of fat may be given without disturbing the fat metabolism, with the resulting formation of ketogenic substances and acidosis. The ratio between fatty acids and glucose should not exceed 1.5 to 1. It is of first importance, therefore, to know that a given quantity of carbohydrate yields in the body 100%

glucose and no fatty acid, proteins yield 58% glucose and 46% fatty acid, and fat yields 10% glucose and 90% fatty acid. With this information it is possible to calculate the diet, so that the ratio of fatty acids to glucose of 1.5 to 1 is not exceeded.

—J. Am. M. Ass., 79, 1073.

DIABETES and pregnancy. Lemann (I. I.), N. Orl. M. & S. J., 1922, 74, 492-499.

Reports a case in which pregnancy caused an improvement in the diabetes. After reviewing the evidence it is concluded that all glucosurias of pregnancy are not diabetes mellitus. Many are innocent renal diabetes. The treatment of the pregnant diabetic is the same as that of the non-pregnant.—F. S. H.

DIABETES MELLITUS in the negro race. Lemann (I. I.), South. M. J. (Birmingham), 1921, 14, 522-525.

The paper is based on a study of the patients admitted to the Charity Hospital of New Orleans from 1898 through 1919—a total of 261,609 cases. In the period from 1898 through 1909 the incidence of diabetes was: white patients, 0.72 per thousand; negroes, 0.47. From 1909 to 1919 the rate was: white patients, 1.4 per thousand; negroes, 0.86. The latter period shows an increase in rate per thousand shared by both races. There was no demonstrable relation between the occurrence of syphilis and diabetes.—J. C. D.

A case of infantile familial DIABETES with rapid progression (*Un cas de diabète infantile familial à marche rapide*). Lereboullet (P.), Blechmann (G.) & Blechmann (J.), Arch. de méd. d. enf. (Par.), 1922, 25, 94-96.

A case of familial infantile diabetes with rapid progression. This was the fifth child in a family of six. The fourth child died at the age of 7 of acute diabetes of 9 months' duration following measles. The patient was watched with care, but no sugar was found in the urine until 15 days after an operation for appendicitis at the age of 9. The development of the diabetes was acute and progression rapid, the total duration of the disease being but 5 weeks. Physical examination was negative but for the glycosuria. The urine showed 80 grams sugar per liter.—C. H. G.

DIABETES and alveolar pyorrhea (*Diabetes e pyorrhéa alveolar*). Lima (C.), Rev. dos Cursos de la Fac. de med. (Porto Alegre, Brazil), 1921, 7, 92-97.

A speculative discussion derived from observation on one case, concerning the possible relation between pyorrhea and diabetes on the one hand and diabetes and the thyroid on the other.—F. S. H.

Sugar content of blood in DIABETES. Lindblom (S.), Hygiea (Stockholm), 1919, 81, 753.

The author theorizes to the effect that hyperglycemia is to a certain extent a useful phenomenon in diabetes. It seems to warn the sugar-forming and sugar-destroying organs that their activities must be regulated.—R. G. H.

Methods of study of early DIABETES. MacLeod (J. J. R.), Canad. M. Ass. J., 1922, 12, 4-6.

The usual methods of measuring the defects of the utilization of carbohydrates of the body are criticised. Blood-sugar curves may be perfectly normal in incipient stages of diabetes. Sugar may be found in the urine of perfectly healthy subjects. The author also defines renal diabetes, and says cases of this disorder must be carefully differentiated from true diabetes.—J. H.

The value of fat in the treatment of DIABETES (*Les graisses dans l'alimentation et le traitement des diabétiques: interpretation physiologique de la cure de jeune*). Maignon (F.), Presse méd. (Par.), 1922, 30, 265-267.

Maignon advocates the extensive use of fat in the treatment of diabetes. He shows that the ingestion of fat reduces both glycosuria and acetonuria and brings out the risk of the development of acidosis, because fats are indispensable for the proper utilization of protein and for the prevention of the abnormal cleavage of proteins which furthers acidosis. His first observation was made on a dog with extremely severe, spontaneous diabetes. It was emaciated and had intense glycosuria as well as a negative nitrogen balance. All of these symptoms disappeared and the animal's general condition improved to a remarkable extent after a few days of exclusive feeding with olive oil. Maignon points out that Allen's starvation treatment of diabetes is known to give excellent results in diabetics who do not show much loss of weight, and that it is far less beneficial to emaciated patients. The physiologic basis of this clinical observation is that the rapid disappearance of glycosuria in well-fed diabetics during starvation is caused by the burning up of the patient's body fat which is present in amounts sufficient to meet all the caloric requirements of the organism. But in the emaciated patient, starvation leads to the burning of the body proteins; as 44% of the proteins are converted into carbohydrates, which the diabetic cannot metabolize in severe types of the disease, glycosuria persists, while the wholesale and inadequate cleavage of proteins furthers acidosis. Several case histories of severe diabetes with improvement amounting to cure under the administration of large amounts of fat are given to illustrate the value of this method of treatment. The therapeutic measures used by Maignon are the following: (1) complete elimination of all carbohydrates from the diet, (2) reduction to a minimum of the intake of protein, (3) maintenance of the normal acidity of the urine by administration of sodium bicarbonate, and (4) adminis-

tration of fat in sufficient amount and in easily assimilated form to furnish the caloric equivalent of the normal carbohydrate requirements. For the latter purpose the following mixture has been found useful: oil of sesame 600 cc., distilled water 300 cc., washing soda 5 grams. This mixture is well shaken at intervals (without heating) during forty-eight hours; it is then allowed to stand for another forty-eight hours, after which the supernatant emulsion is poured off. To the emulsion which is partly saponified 20 grams of neutral glycerine as well as 0.02 gram of vanilla and "half a drop" of bitter almond oil are added to correct the taste. Maignon also points out that the unsatisfactory results of fat-feeding to depancreatized dogs, reported by Allen, are readily accounted for by the fact that removal of the greater part of the pancreas leads to disturbances of fat metabolism, because the pancreas plays an important part in the metabolism of fats, but that the activities of the pancreas, with regard to the handling of fat, are rarely curtailed in the spontaneous types of diabetes.—G. L.

The nitrogen requirement for maintenance in DIABETES MELLITUS.

Marsh (P. L.), Newburgh (L. H.) & Holly (L. E.), Arch. Int. Med. (Chicago), 1922, 29, 97-130.

Very carefully controlled dietary experiments on 12 diabetics were performed to determine the state of nitrogen equilibrium, the nitrogen in the food being balanced against the nitrogen in the urine and stools. The treatment used was the low protein, high fat, low carbohydrate diets previously described by Newburgh and Marsh, and concerning which there has been much controversy. The authors came to the following conclusions. Nitrogen balance can be established in the diabetic according to the laws of applicable to the normal subject provided his total caloric requirement can be satisfied. This implies that he can burn enough glucose to metabolize fat. Diabetics who cannot burn this small amount of glucose are extremely rare. Protein metabolism above the minimal is undesirable in the diabetic because of the great glycogenic property and the large specific dynamic action of protein. Excessive protein metabolism results from a diet containing either too much protein or too few total calories.—H. L.

DIABETIC coma cured by intravenous injection of bicarbonate of soda (Coma diabétique guéri par le bicarbonate de soude en injections intraveineuses). Minet (J.) & Boulet (L.), Réunion méd. chir. des hop. de Lille, 1922, June 19; abst., Presse méd. (Par.), 1922, 30, 683.

A case is reported of a young girl of 20 years who had unrecognized diabetes for about 5 months. There was first vomiting and diarrhea, then torpor and finally absolute coma; respiration was the only sign of life. One intravenous injection of 500 cc. of a solu-

tion of bicarbonate of soda to 300 to 1,000 after 13 hours of coma resulted in recovery during the course of the injection. The result, maintained by enema of bicarbonate of soda and by second intravenous injection, appeared to be definite; the acetone odor disappeared shortly afterwards; the girl recovered complete consciousness in 6 days. The seventh day she slowly died, but without coma or new signs of acetonuria, showing a group of symptoms indicating acute adrenal insufficiency. The authors call attention to the extreme rareness of diabetic coma that is not immediately fatal.

—R. G. H.

DIABETES in children (*Formes cliniques du diabète sucré chez les enfants*). Nobécourt (P.), *Médecine (Par.)*, 1922, 3, 834-838.

Nobécourt warns not to mistake for glycosuria the alimentary lactosuria of infants with gastro-intestinal derangement. The mild form of diabetes in children can generally be cured by restricting carbohydrate intake, but sometimes it persists unmodified and without aggravation up to adult life. The child develops apparently normally. Sometimes the mild form changes to the grave form or the diabetes may be grave from the start, with a tendency to denutrition or to hypotrophy or both. The prognosis should always be reserved; the effects of treatment will generally tell the story.

—J. Am. M. Ass., 79, 1554.

(DIABETES) Study of blood sugar curves following a standardized glucose meal. Olmsted (W. H.) & Gay (L. P.), *Arch. Int. Med (Chicago)*, 1922, 29, 384-399.

More than 200 cases were studied critically. The interpretation of the values of sugar curves depends on the following factors: (1) the technic of administration of the glucose meals; (2) the collection of blood samples; (3) the method of doing the blood sugar determination, and (4) the wide application of the test so as to learn the many factors which influence these curves. The standardized Janney glucose meal was used. Three types of curves are described: normal, showing a normal fasting blood sugar, a normal rise after the glucose meal, and a return to normal or slightly subnormal at the end of two hours; the subnormal curve, showing a hypoglycemia or normal fasting sugar and no hyperglycemia following the glucose meal; the sustained hyperglycemic curve, divided into two groups, those showing hyperglycemia the second hour but with a return to normal levels the third hour, and those showing hyperglycemia at the end of three hours. In hyperthyroidism marked hyperglycemia resulted after the glucose meal, with return to normal level in three hours. There is no relationship between the height of metabolism (basal metabolic rate) and the height of the blood glucose curve. Hypothyroid cases constantly showed hypoglycemic curves, probably due to increased sugar storage, rather than delayed

intestinal absorption. Hypopituitarism produced hypoglycemic curves. The high sustained curve even in mild diabetes was invariably found. Two cases of renal diabetes gave flat curves. No prediction as to the type of curve in mental disease can be made. Normal or flat or high curves may be obtained in hysteria, neurasthenia, dementia, praecox, hypochondria, etc. Abnormal curves, though quite inconstant, may be obtained in chronic infections, malignancy, pernicious anemia, leukemia and Hodgkin's disease.—H. L.

Significance of DIABETES MELLITUS in mental disorders. Pike (H. V.), J. Am. M. Ass. (Chicago), 1921, 76, 1571-1572.

The relation of mental disorders to disturbances of metabolism, especially glycosuria, is briefly discussed. Pike reports two cases of diabetes mellitus occurring in patients suffering from mental disease, but in which the somatic condition was in no sense contributory to the psychosis. A third case presented the picture of a psychosis consequent to the development of diabetes mellitus.

—W. M. A.

Clinical importance of BLOOD SUGAR (Zur Klinischen Bedeutung des Blutzuckers). Schirokauer (H.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1034.

Offenbacher and Hahan have stated that blood sugar must be estimated in the blood and not in serum. Schirokauer shows that this gives rise to serious mistakes, and that only the study of the amount of metabolizing glucose is not the same as all metabolic levels but may be increased by measures designed to depress the basal metabolic rate.—F. S. H.

(ENDOCRINE GLANDS) Choline as hormone of intestinal peristalsis. VII. Choline content of the alimentary canal in hunger and after morphine (Choline als Hormon der Darmbewegung. VII. Cholingehalt des Magendarmkanales im Hunger und nach Morphin). Arai (K.), Arch. f. d. ges. Physiol. (Berl.), 1922, 195, 390-409.

The choline content of the stomach and small intestine was determined by one-hour dialysis and the action of the concentrated dialysate on rabbit's intestine was studied. Normal cats gave very constant values. The amount present in cats' stomachs and intestines after 17, 48 and 90 hours' hunger was the same as immediately after feeding. The choline content in dogs' stomachs and intestines is distinctly decreased after subcutaneous injection of 6 mg. per kg. of morphine, but there is no difference in the sensitive-

ness of isolated intestinal strips of normal and morphinized dogs to stomach- and intestine-dialysates of normal and morphinized dogs. In cats, 6 mg. per kg. of morphine produces a slight decrease of the stomach-choline, 20 mg. per kg., a marked decrease in both stomach and intestine content; 1 mg. per kg. is without effect. After colocynth-diarrhea, the choline-content is not altered in cats. Stopping the diarrhea by morphine, with complete intestinal standstill slightly lessens the stomach-choline, but does not affect the intestinal content; such action cannot be due to choline-loss.

—A. T. C.

(GONADS) ENDOCRINE tissue in the TESTICLE of the urodele (Sur l'existence et le rôle d'un tissu endocrinien dans le testicule des urodèles). Aron (M.), Compt. rend. Acad. d. sc. (Par.), 1921, 173, 57-59.

The authors believe that this tissue is analogous to the interstitial tissue of mammals and birds. They describe its histological structure; it begins to form before spermatogenesis occurs, and the nuptial period coincides with its fullest development. Destruction by cautery leaving the seminiferous tubes intact leads to a disappearance of sexual appetite and of secondary sexual characters.

—Physiol. Abst., 6, 384.

(ENDOCRINE GLANDS) The foundations of hormone therapy (Grundlagen der Hormonentherapie). Asher (L.), Schweiz. med. Wchnschr. (Basel), 1920, 50, 1057-1060.

Hormone therapy has its foundation in the totality of scientific biology, particularly in the biochemical and biophysical methods of practical physiology. On the basis of this definition Asher presents a generalized discussion of the action of the hormones, in which the secretions of the thyroid, adrenals, hypophysis, gonads, etc., are emphasized.—F. S. H.

The action of extracts and products from the glands of INTERNAL SECRETION on the isolated uterus, particularly after total castration (Action d'extraits et produits dérivés d'organes à sécrétion interne sur l'utérus isolé, particulièrement après la castration totale). Athias (M.), Arch. internat. de pharm. et therap. (Brux. & Par.), 1920, 25, 423-452.

The uterus from rabbits, cats, dogs and hedgehogs shows the same diminution of automaticity after total castration as does that of the guinea-pig. The normal isolated uterus from non-castrated animals reacts through its tonic function to adrenin and adrenal extracts, to extracts of the hypophysis and ovary by transitory phenomena which are often accompanied by modifications in clonic function. The response to adrenin is that already described by other workers. The response to extracts of the hypophysis is a

shortening. Ovarian or corpus luteum extracts act as stimulants. The reaction to the various substances is the same for the uterus from the normal and from the castrated animal.—F. S. H.

The relation of the INTERNAL SECRETIONS to metabolism. Aub (J. C.), J. Am. M. Ass. (Chicago), 1922, 79, 95-98.

In a survey of the literature with a brief reference to work from the author's laboratory, already reported and soon to be published, Aub reaches the following conclusions. Apparently the two glands which most influence the total metabolism are the thyroid and the suprarenal (probably by epinephrin). The mechanisms of their actions are independent of each other. The theory is advanced that the suprarenals exert acute effects, while the thyroid is the more sluggish regulator of the metabolic rate. The method of action of thyroxin and epinephrin is probably a direct one on the tissue cells.—W. M. A.

(ENDOCRINE) Case of hirsutism with melancholia (Un cas d'hirsutisme avec mélancolie). Ballif (Charlotte), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1920, 2, 43-44.

The relation of the ENDOCRINE glands to heredity and development. Barker (L. F.), Science (N. Y.), 1922, n. s. 55, 685-690.

A general address given before the Eugenics Research Association.—F. A. H.

ENDOCRINOLOGY. Barker (L. F.), J. Am. M. Ass. (Chicago), 1922, 79, 89-91.

The conception that the endocrine organs are linked together so as to form a system of reciprocally dependent organs (homonopoietic system), Barker states, has gradually gained general credence, not only among clinicians, but also among physiologists and pathologists. And it must be admitted that there is considerable evidence in favor of the existence of such a correlative interdependence among the several incretory glands. Physiologists, through their experiments, have adduced many facts that point to manifold interrelationships between the glands of internal secretion. And clinical-pathologic studies have shown that uniglandular endocrinopathies are rare, whereas pluriglandular endocrinopathies are common. In exophthalmic goiter, for example, we see not only diffuse hyperplasia of the thyroid gland, but also, not infrequently, hyperplasia of the thymus as well as signs of insufficiency of the gonads. In Froehlich's syndrome, to cite another instance, we see not only the signs of a disorder of the hypophysis cerebri, but also evidences of hypogenitalism. It seems very probable, therefore, that in the chemical integration of the bodily activities a certain co-operation among the endocrine organs is essential. The homonopoietic system is concerned as a whole. It, like the nervous system, helps to correlate

the partial systems of the body into a harmonious unity. Though the principles of therapy for the endocrine diseases are not hard to grasp, the application of these principles in practice is compulsorily restricted, owing to the fragmentary character of existing knowledge. When, through constitutional deficits, or, under the influence of unfavorable conditions disharmonies of the hormonopoietic system arise, and evidences of hyperfunction, of hypofunction or of dysfunction, of one or more of the single endocrine organs appear, therapeutic intervention may become desirable. When a disease process has already developed; in other words, when an endocrinopathic personal variant has become incapable of satisfactory adaptation (state of irresponsivity), the physician may attempt to decrease function here, to increase function there, or to modify function elsewhere, in the hope of restoring balance, and of bringing the powers of personal adaptation again within the limits of normal responsibility. Thus, in hyperfunction of an endocrine organ it may

be to excise a portion of it, or to curtail its activity by limiting its blood supply (ice-bag; arterial ligation); or, by means of a depressive radiotherapy or chemotherapy. On the other hand, in the case of hypofunction, it may become desirable to resort to organ transplantation, or to a substitution therapy (administration of gland substance, or of gland extracts, or of isolated hormones), or to attempt to revive a falling function by a dietetic hygienic regimen, or by mild stimulative radiotherapy.—Courtesy Am. M. Ass.

ENDOCRINE growth disturbance; acromegaly, gigantism, dwarfism.
Bassoe (P.), Med. Clin. N. Am. (Phila.), 1921, 5, 85-100.

A practical review of this subject, with mention of a few illustrative cases. Though pluriglandular dysfunction may lead to growth disturbances, the most striking cases are due to pituitary disease with or without thyroid and gonadal involvement. A lack of hypophyseal secretion, as in the case of teratoma or congenital cyst of the organ, leads to so-called hypophyseal dwarfism with arrested sexual development and ossification (infantilism). Infantilism, however, may occur without stunting of growth, and indeed may occur with gigantism. Castration early in life presents disproportionately long extremities, small head with compensatory enlargement of the hypophysis, a small thyroid, a thymus persisting beyond the normal period, a thick growth of hair on the head but with lack of beard and pubic hair, small larynx and absence of the usually expected vocal changes. In gonadal deficiency due to congenital tumors of the testicle, hyperpituitarism may occur, resulting in extremely rapid growth as in the case of Sacchi, a boy who was also sexually mature at nine years. By eunuchoidism is meant a developmental disorder resulting from defective testicular interstitial glands, in which the characteristics of the eunuch are also present; excessive deposits of fat in these cases implicate the hypophysis, and carious

teeth with marked skin changes involve the thyroid. With regard to acromegaly and gigantism, Bassoe lays down the following general rules. 1. There are no "normal" giants. 2. All cases of gigantism belong in one of the following groups: (a) gigantism with infantilism, (b) gigantism with acromegaly, (c) gigantism with infantilism and acromegaly. 3. When gigantism and acromegaly are combined, the former condition appears first. 4. About half of all reported giants have had acromegaly. 5. Both gigantism and acromegaly are due to hyperfunction of the hypophysis; when this occurs in childhood or early youth a giant is produced, while after the epiphyseal lines have closed, acromegaly results. Aside from indications of pituitary disease, there are, in acromegaly, amenorrhea and other genital disorders, abnormal pigmentation, growth of hair and other skin changes implicating the gonads, the adrenals and the thyroid. In addition to extreme skeletal growths, the enlargement of the hypophysis per se gives rise, because of pressure, to changes in the visual fields, and occasional atrophy and blindness, and in extreme cases to the usual symptoms of brain tumor. The prognosis of acromegaly varies with the form of the affection. The severe form is fatal in a few years; the usual chronic form terminates in from eight to thirty years, while the benign form does not shorten life. The disease may be active for a few years and then remain stationary during the remainder of the patient's life, in which cases the age of one hundred years is known to have been reached. Treatment during the active stage is futile, and the administration of glandular extracts may aggravate rather than relieve the symptoms. If later there are evidences of hypopituitarism, pituitary opotherapy is indicated. X-ray treatment has been tried with asserted success in many cases. Surgery has now attained a place and deserves attention in active cases. The author classifies dwarfs as follows: 1. Proportionate dwarfs: (a) Primordial dwarfs (essential microsomia), (b) Hypophyseal dwarfs; and 2. Disproportionate dwarfs: (a) Achondroplasia (chondrodystrophia fetalis), (b) Stunting of growth from rickets or Pott's disease, (c) Cretinism, and (d) Congenital syphilis. Primordial dwarfism is congenital; the cause is unknown, and no endocrine or other etiological factor has so far been demonstrated. These individuals appear like normal people seen through the large end of a telescope. Though a "normal" giant does not exist, we must admit the existence of a "normal" dwarf. The hypophyseal dwarf is the antithesis of the acromegalic giant; they are small but proportionate, have too little hypophysis tissue, and do not acquire normal sexual or osseous development. Cases of achondroplasia are also congenital, presenting a relative shortness of the extremities with relatively large, broad heads and a tendency to precocious sexual development.—I. B.

(ENDOCRINE) The effects produced by extracts of PINEAL, ADRENALS, LIVER, TESTICLE, and OVARY, injected into the lateral

ventricles of the brain (Effets produits par les extraits de la glande pinéale, des capsules surrénales, du foie, du testicules et de l'ovaire injectés dans les ventricules latéraux du cerveau). Battelli (F.) & Stern (L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 755-756.

In rare cases extract of beef pineal produces in the dog a state of excitation immediately after injection, which soon gives way to somnolence and true sleep, analogous to that produced by the hypophysis but less pronounced. After several hours the animal recovers its normal aspect. The temperature is slightly elevated. In the guinea pig the rise is preceded by a transient fall. In the guinea pig the suprarenal cortex often causes a slight initial excitation followed by depression more or less prolonged. The temperature is lowered. Death often occurs in 24 hours. In the dog there is no immediate effect, but sleep soon comes on, lasts several hours, and gradually disappears. In the guinea pig the suprarenal medulla causes paralysis varying with the dilution. The temperature is low-

The same is true for the dog: somnolence, slow respiration, tion of temperature, recovered from in a few hours. These ts are probably due to adrenalin. Extract of beef liver causes most immediately muscular contractures and subsultus either spontaneous or upon excitation. Soon the dog rests upon its flank, but does not sleep; the reflexes are sometimes exaggerated. Recovery occurs in a few hours. Boiled extract acts more rapidly than fresh extract. The guinea pig testicle produces in the guinea pig either immediately or after several minutes, a state of agitation, vivacity, exaggeration of sensibility with a tendency to contractures. Recovery is rapid. In the dog there are no appreciable effects. Extract of cow's ovary gives inconstant effects—sometimes no result, sometimes excitation. In some dogs there was vomiting, and in one intense polypnea. The temperature was augmented. In a general way the glands may be classified into those predominantly depressing: the posterior lobe of the hypophysis, the pineal gland, the suprarenals; and those whose action is predominantly exciting: the thyroid, liver, spleen, testicle and ovary.—T. C. B.

ENDOCRINOLOGY: The neurologic phase. Bitler (C. C.), *Proc. Indiana State M. Ass.*, 1922, Sept. 28-30.

For practical purposes, the human nervous system may be divided into three levels of activity—the vegetative, the sensorimotor and the psychic. In the region of the vegetative neurology a rich variety of disturbances is found, involving the glandular, gastrointestinal, genito-urinary, vascular, respiratory, muscular, cutaneous and bony systems. In addition, there are certain complex groups involving, for the most part, the glands of internal secretion—the endocrinopathies. Clinical syndromes resulting from disease of the glands of internal secretion are almost always pluriglandular. There

is a close relationship between the glands of internal secretion and their products, and the vegetative nervous system.

—J. Am. M. Ass., 79, 1545.

The diagnostic and therapeutic rôle of the ENDOCRINES in functional diseases. Blumgarten (A. S.), N. York M. J. (etc.), 1922, 115, 393-401.

After reviewing the history and establishing the rationale of endocrinology, the author proceeds to apply its principles to the pathogenesis of functional diseases. In discussing gastric neuroses he cites a case in which definite gastric symptoms and later frank thyroidism developed following a hold-up scene. "The sudden shock disturbed the cerebral and adrenal cortical relationship, producing adrenal insufficiency with compensatory hyperthyroidism manifesting itself at first by the gastric symptoms and later by the hyperthyroidism in addition." In a second case a man developed hyperthyroidism a month after recovery from scarlet fever. He suffered from gastric neurosis and hyperacidity. "In this patient the adrenal injury produced an adrenal insufficiency with compensatory hyperthyroidism, which began with gastric symptoms." "Cases of hyperacidity should be treated as cases of hyperthyroidism." In addition to rest, diet and stabilization of the emotions the author gives adrenal cortex—"the value of which I cannot emphasize too much"—"to overcome the underlying hyperthyroidism, for by overcoming the hyperthyroidism the vagotonic state is relieved. In the cases of anacidity and achylia gastrica, brilliant results are obtained by recognizing the thyroid deficiency and feeding these patients small doses of thyroid extract." Neurasthenia, or "adrenalasthenia," is characterized by profound asthenia, lack of sympathetic tone, gastric neuroses and low blood pressure. "Consequently, it is being more and more appreciated that what we are dealing with in neurasthenia is an endocrine disturbance characterized by an adrenal insufficiency." Amenorrhea may result because of thyroid deficiency, dominance of the adrenals, in which case there are more or less masculine tendencies, and because of pituitary insufficiency; there is also loss of ovarian function. Metrorrhagia and menorrhagia occur either associated with hyperthyroidism or pituitary manifestations. Those of the first class should be treated for hyperthyroidism by adrenal cortex, atropin and sedatives. Those of the second class are often relieved of their pituitary headaches and dysmenorrhea by the use of pituitary extract, atropin and sedatives. Primary ovarian developmental deficiencies are difficult to recognize. "They are frequently associated with masculine characteristics. The secondary deficiencies, however, are usually associated with evidence of pituitary deficiency, usually in the Froehlich type of patients, associated with amenorrhea and infantile uterus." "The results of therapy in these cases cannot be predicted, and for the most part are unsuccessful."—H. W.

(**ENDOCRINE**) Mode of action of **SECRETIN**. Dalmau (M.), Treb soc. biol. Barcelona, 1917, 19, 327; *Physiol. Abst.*, 1919, 2, 527.

The liver had no influence on the quality and quantity of the pancreatic juice, which was produced by administration of dry secretin.—Quoted.

(**ENDOCRINOLOGY**) Nomographic charts for the calculation of the metabolic rate by the gasometric method. Boothby (W. M.), & Sandiford (R. B.), Boston M. & S. J., 1921, 185, 337-354.

Presentation of nomographic charts by which the calculation of the basal metabolic rate from the data obtained by the gasometer method can be made graphically in less than 5 minutes without the use of logarithms. The methods of construction and use of nomographic charts are given in detail.—H. W.

(**ENDOCRINE**) The alchemy of animal extracts. Bowers (E. F.), Trained Nurse [etc.] (N. Y.), 1921, 67, 37; 119.

Reference verified from *Index Medicus*.

The biology of the **ENDOCRINE** system. Brown (W. L.), N. York M. J. [etc.], 1922, 115, 373-376.

Save for the medulla of the adrenals, the islets of the pancreas and the doubtful instance of the pineal, the endocrine glands represent modified nephridia. In worms and lowly arthropods paired nephridia open externally from each segment. When appendages are developed these form the coxal glands at their base. With the modification of these appendages the corresponding glands become modified. The prosomatic ones become the pituitary, the mesosomatic become the tonsils, thyroid, parathyroids and thymus, and the metasomatic ones the adrenals. Only the hindmost retain their original excretory function, becoming conglomerated into the metanephros, and instead of opening separately to the surface they drain into the metanephric duct. The pronephros and the mesonephros of the primitive vertebrate kidney vanish in so far as the latter gives rise to interstitial cells, and their ducts are annexed by the gonads. The close anatomical relationship between the kidneys and the adrenals is thus comprehensible. The formation of the new alimentary tract (theory of Gaskell) and the plural folds shut off the anterior nephridia from the surface and force them to become ductless. Nephridia containing lymphatic structures and some of these which had thus been shut off develop this lymphatic element at the expense of the glandular, but in their phagocytic properties still show their association with excretory functions. Others acquire new secretory functions, though in some instances still showing chemically a vestige of their primitive secretory action. The endocrine functions which are the specialization of the old chemical method of stimulation and defense become concentrated in these structures

which perforce have to change their functions. Gradually these chemical methods come largely under control of the sympathetic nervous system which correlates them and enables them to be brought rapidly into action either for the ordinary processes of metabolism or for external and internal defense.—H. W.

A critical consideration of ENDOCRINE therapy. Cannon (W. B.), *Boston M. & S. J.*, 1922, **187**, 163-164.

This article is a brief discussion of the fallacies on which some of our present endocrine treatment is based; together with a plea for careful and critical use of endocrine products. No new data are given.—J. C. D.

Some conditions controlling INTERNAL SECRETION. Cannon (W. B.), *J. Am. M. Ass. (Chicago)*, 1922, **79**, 92-95.

No one, says Cannon, may now question the great influence of the glands of internal secretion on important physiologic processes. There appears to be a tendency just now, however, to pay these glands not only respect, but also deference, homage and a blind worship. The physiologist regards the body as a system of organs, each performing its service, each influenced by other organs and capable in turn of influencing other organs, and each having a use and a value only in relation to the others. Questions now arise regarding the real status of the glands of internal secretion. If they have not the dominant position commonly assumed for them, how may they be subordinated? What influences can be brought to bear on them in such a way as to modify their activity? These are important questions to have answered—important because of the profound effects which the ductless glands themselves are capable of exerting. Cannon presents some of the evidence for physiologic control of the internal secretions. He points out that bodily functions are managed by a system of checks and balances—by mutual adjustments, such as those between antagonistic muscles, and by maintained equilibria, such as those between material income and outgo, and between acid and base in the blood. If the endocrine glands are regarded as the regulators of important physiologic processes, normally they are well regulated regulators.

—Courtesy Am. M. Ass.

Studies on the conditions of activity in ENDOCRINE GLANDS. XI. Further evidence for reflex and asphyxial secretion of ADRENIN. Cannon (W. B.) & Carrasco-Formiguera (R.), *Am. J. Physiol. (Balt.)*, 1922, **61**, 215-227.

After cutting the hepatic nerves blocking the venous path from the adrenals in such a way that the only change is a shutting of the adrehal blood from the circulation, the reflex response is prevented. If the venous block is removed the response is again ob-

tained. Asphyxia for 45 seconds fails to produce an increased rate of heart beat if the venous flow from the adrenals is prevented.

—T. C. B.

Hypofunction and hyperfunction of the DUCTLESS GLANDS. Carlson (A. J.), J. Am. M. Ass. (Chicago), 1922, 79, 98-104.

No single phase of endocrine dysfunction, Carlson asserts, is satisfactorily worked out today, either clinically or experimentally. He presents the established facts and what appear to be obstacles to progress—baseless speculation and uncritical practice. The credit for progress made and the blame for errors committed are shared by the clinical and laboratory groups. Failure to recognize the complexity of every endocrine problem is a serious obstacle to victory. Following the hormone theory alone may, in the case of some of the ductless glands, lead way off the main road. Carlson believes that much of the glandular therapy of today, however harmless to the patient, injures the good name of the medical profession with intelligent laymen. He says: "We cannot practice quack methods and escape the just censure of society. The quack diagnoses every ailment with ease, and offers remedies for every disease with assurance. The good physician knows that he is neither omniscient nor omnipotent in the field of disease; and the educated layman knows this as well as the physician. Then, why pretend? Bluff may succeed for a time, but honesty is better for society; and what is best for society is best for the medical profession."

—Courtesy Am. M. Ass.

ENDOCRINE tumor of the appendix (*Des tumeurs ENDOCRINES de l'appendice*). Cazin, Paris Chir., 1919, 11, no. 3; abst., Presse méd. (Par.).

In 1914 Masson showed that two kinds of cancer of the appendix could be distinguished: cylindrical epithelioma of the ordinary intestinal type, and tumors proceeding from the endocrine gland of the intestine. The latter are different in that they have an abnormal proliferation of the submucous tissue, made up of special "argentaffines" cells. These cells are normally scattered throughout the small and the large intestine and altogether form a diffuse endocrine gland of endodermic origin. Tumors derived from this tissue are of a compact texture; they are formed from connected, intertwined, anastomoses, made up of small polygonal cells. Sometimes these cells disclose their endodermic origin by vestiges of cavity formations, covered by cylindrical epithelium; in other cases they grow in compact groups. In spite of these characteristics of malignant histology these small neoplasms can be classed among the benign tumors. Cazin operated upon a tumor of this kind in a young woman of 28 years whose clinical history was that of ordinary chronic appendicitis. The appendix appeared normal exteriorly, but

showed on section a nodule, about 3mm. in diameter, between the muscular and the mucous membrane. Under the microscope this nodule showed all of the characteristics of the endocrine tumor described by Masson.—R. G. H.

(ENDOCRINE GLANDS) Congenital anlagen in pluriglandular insufficiency (Zur Frage der kongenitalen Anlage bei pluriglandulärer Insuffizienz). Curschmann (H.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.), 1920, 59, 264.

The author disputes the statement of Krabbe that his two cases of congenital pluriglandular insufficiency are unique in the literature, and proceeds to cite an imposing list of such abnormalities. Cited from Schweiz. med. Wchnschr. (Basel), 1922, 52, 662.

—F. S. H.

(ENDOCRINE GLANDS) Osteitis deformans: Paget's disease of the bones. DaCosta (J. C.), Tr. Coll. Phys. (Phila.), 1920, 42, 52-67.

Paget's disease is apparently a distinct malady though closely related to osteomalacia and von Recklinghausen's disease. Late cases of Paget's disease show metabolic changes the reverse of those found in osteomalacia. Endocrine disturbances may be an etiological factor.—Chem. Abst., 16, 2911.

The ENDOCRINES and their influence on the skin. Davidson (A.), Calif. State J. M. (San Fran.), 1921, 19, 248-250.

The author concludes that only those glands developed from the same somatic layer as the skin directly affect it; also, that those glands which originally discharge their secretions into the digestive tract alone afford products that are effective therapeutically when administered by mouth.—H. W.

The ENDOCRINE ORGANS, and the utilization of their products in pharmacy. Dryerre (H.), Pharm. J. (Lond.), 1922, 108, 265-266; Chem. & Drug. (Lond.), 1922, 96, 418.

An address on the functions of the ductless glands of the body.
—Chem. Abst., 16, 2575.

ENDOCRINE ADIPOSITY. Engelbach (W.), Med. Clin. N. Am. (Phila.), 1922, 6, 1-29.

An excellent paper dealing with the evaluation of obesity as a diagnostic sign of certain ductless gland disorders. Obesity and undernutrition are not necessarily due to heredity, deficient or excessive exercise, improper feeding, and the like. The evaluation lies not in the amount of food taken, but in the amount stored in the body or catabolized and excreted, which produces the balance in weight. Though the internal secretions play an important part in

the regulation of the rate of metabolic activity, we find that in obesity in patients with uncomplicated pituitary or gonad disorder, metabolic determinations vary but little from the normal. With a view to throwing additional light upon the etiology of adiposity in pituitary and gonad insufficiencies, studies of the blood fat are being made, for it is possible that the cause lies in deranged fat metabolism. The basis for the following deductions regarding these endocrinous adiposities is the correlation of the studies made by the author and Dr. John L. Tierney of 1995 cases of disorders of the ductless glands. Two aides were depended upon in diagnosis: (1) the age incidence of the obesity; (2) the localization and distribution of the obesity.

Infantile adiposity or adiposity at birth is seen in cretinism and frequently appears in the history of adult hypothyroid females. Adiposity, late dentition and late locomotion and speech are sufficient reasons for placing an infant upon treatment for hypothyroidism. Hypothyroid babies do not carry an excessive weight into their early childhood, hence children past three or four with adiposity probably are not hypothyroid, and if hypothyroid, have an added hypopituitarism. Juvenile adiposity (between the fourth and fourteenth year) is due to hypofunction of the posterior lobe of the pituitary. The history of such patients usually reveals a normal birth and development up to the age of 4 or 5. Between this age and adolescence they suddenly take on an unusual adiposity out of proportion with their age and height. Otherwise the patients appear normal, and the mentality is normal, or even precocious. Adult adiposity may be due to disorders of the pituitary, the thyroid or the gonads, or a combination of these. Aside from early castrates and classical eunuchs (in which the adiposity is located over the trochanter area), adiposity due to insufficiency of the gonads rarely occurs before the age of 34 or 35. Thyroid and pituitary adiposity may occur at almost any age, but in cases occurring past 30, of a duration of a year or two, there is a likelihood of a pluriglandular involvement secondary to a uniglandular disorder.

The distribution of the adiposity is of diagnostic value. Thyroid adiposity presents the characteristic dorsal hand padding and supraclavicular padding with evenly distributed adiposity. In infants and juveniles the hand and cervical padding may be absent, while in adults it may be transient. Pituitary adiposity in childhood and adult life is located about the hip and shoulder girdles. The pelvic girdle adiposity extends from the navel down to the juncture of the middle and lower thirds of the thigh. The shoulder girdle is often most marked over the deltoid region. Considerable adiposity about the lateral aspects of the thorax is likewise seen. Cases with deficiency of the anterior lobe of the pituitary with infantile genitalia may present some mammary adiposity not quite so marked as in primary gonad insufficiency. The forearm, hand, leg, foot, and the

cervical regions are quite free from infiltration. There is comparatively little mons veneris padding excepting in cases of secondary hypogonadism due to anterior pituitary insufficiency. In gonad insufficiency up to the age of 34 or 35, there is complete absence of adiposity, except about the trochanteric regions. In early castrates in both sexes, there is a tendency to overgrowth of the long bones. True gonad obesity begins to appear at 34 or 35, consisting of disproportionate mammary enlargement, an apron of mons veneris, and a fullness of the thighs. Pluriglandular obesity consists of a blending or fusing of a number of these typical adiposities in a single individual. The diagnosis depends largely upon a careful history, with special attention to age incidence, localization and distribution of the adiposity, and the fact that the disorder begins as a uniglandular condition.

Treatment to yield results must be instituted early—when only one gland is affected, with the purpose of stimulating it into normal physiological activity. Failure in treatment is due to late diagnosis and lack of a proper sense of therapeutical indications. In cases diagnosed early, treatment may fail for the following reasons: (1) the digestion of much of the ductless gland preparations in the stomach; (2) insufficient dosage; (3) too long intervals between hypodermic injections; and (4) the administration of an insufficient amount of the active principle of the glands subcutaneously or intravenously. Digestion by the stomach may be avoided by the use of salol-coated or creatinin-coated capsules. With the exception of thyroid preparations, opotherapy per oram is unsatisfactory. Thyroid administration in hypothyroidism should be guided by the temperature, weight, and the pulse rate of the patient. In pituitary deficiency, pituitrin is administered in gradually increasing doses until the "intestinal reaction" is produced; dosage is then continued. If after two or three months of intensive treatment there has been no decided improvement, the case may be considered as not amenable to opotherapy. Cases of gonad insufficiency in the male do not yield to treatment by the various orchic substances, nor do they respond to pineal or pituitary treatment. In female gonad insufficiency, large doses of entire ovarian substance administered 4 or 5 times daily result in improvement. In adiposity due to pluriglandular disorder, the treatment will depend largely upon the judgment of the experienced endocrinologist. Early, prolonged uniglandular treatment in pluriglandular disorders is an aid in estimating therapeutic indications and in helping to fix the diagnosis in complex clinical pictures. In addition to endocrine treatment, the necessary dietetic, hygienic, and hydrotherapeutic measures should be employed.—I. B.

Physiognomy of ENDOCRINOLOGY. Fridenberg (P.), N. York M. J. [etc.], 1922, 115, 413-415.

A sketchy discussion in which the author transfers the explanation of facial characteristics from the school of phrenology and physiognomy to the newer school of endocrinology.—H. W.

The newer critical phase of ENDOCRINOLOGY (*L'endocrinologia nella sua recente fase critica*). Frontali (G.), Riv. di clin. pediat. (Firenze), 1919, 21, 100.

According to Gley an organ can be classified as a gland of internal secretion only when the relation of its secreting elements to the blood stream is established, when the secretion can be chemically determined in the blood, and when the venous blood from the organ has a specific physiological action. An observation of Quinquaud is cited in which the blood of the inferior vena cava was found not to contain adrenin, and consequently this substance is to be looked on as an excretion and not as a physiological secretion. Frontali thinks the criticism is too inclusive. For example, it is impossible at present to detect in the blood the products of the thyroid gland activity, yet thyroid medication is of established benefit in certain well-known conditions. On the other hand, perhaps it is true that the effectiveness of the thyroid extract is referable to the storage of the active principle in the follicles in noteworthy amounts while this may not be the case in the other glands.—F. S. H.

ENDOCRINOLOGY: The surgical phase. Gatch (W. D.), Proc. Indiana State M. Ass., 1922, Sept. 28-30.

The most important aspect of endocrinology from the standpoint of the surgeon is the uncertain and fragmentary state of our knowledge about it. We must move cautiously. Therefore, in the diagnosis of supposed endocrine disease, or in the operative treatment, we must employ the most rigid criteria of judgment, and not allow theories of endocrine function to influence us, for today the truth of these theories is almost without exception undemonstrated. These conclusions do not dispute the great physiologic importance of the endocrine glands, and should not discourage study of their functions.—J. Am. M. Ass., 79, 1545-1546.

(ENDOCRINE) A metabolic study of progressive pseudohypertrophic muscular dystrophy and other muscular atrophies. Gibson (R. B.), Martin (F. T.) & Buell (M. V. R.), Arch. Int. Med. (Chicago), 1922, 29, 82-96.

Seven cases of progressive pseudohypertrophic muscular dystrophy in boys and two adult male cases formed the material for careful metabolic study. One case each of myasthenia gravis, muscular atrophy following acute anterior poliomyelitis, and myositis ossificans were also studied. Endocrine disturbance in progressive pseudohypertrophic muscular dystrophy is indicated by the hereditary character of the condition, the metabolic abnormalities, the

occasional recovery at puberty when glandular readjustments occur, reported improvement following endocrine therapy in some cases, and the development of the disease in polyglandular dystrophies, notably in association with dystrophia adiposogenitalis. Necropsy findings with special reference to ductless glands are urgently needed to elucidate further the pathogenesis of the condition. The authors review the literature covering the metabolic investigations of this disease, and summarize the outstanding features (corroborated by their own investigations) as follows. Those associated with the atrophic condition of the muscles, and which are intensified as the atrophy progresses are lowered creatinin excretion and creatinin coefficient, creatinuria, recovery in the urine of ingested creatin and creatinemia, though high blood creatins are not a constant finding. In disturbances of carbohydrate metabolism of endocrine origin the usual but not constant findings are hypoglycemia and deficient glycogenesis following moderate glucose ingestion, commonly without glycosuria. The differential diagnosis of progressive pseudohypertrophic muscular dystrophy, myasthenia gravis, and progressive muscular atrophy may be checked by the metabolic and blood findings, as indicated in following table:

	Creatinuria	Blood Glucose	Glucose Tolerance
Progressive pseudohypertrophic muscular dystrophy	Present	Low	Diminished
Myasthenia	Absent	Low or normal	Diminished
Progressive muscular atrophy	Present	Normal	Normal
			—H. L.

ENDOCRINE types of dysmenorrhea. Godbey, West Virg. M. J. (Huntington), 1921, 17, 108.

Endocrine factors play an important part in menstrual life. The hypothyroid girl is small and menstruates very early and there is prolonged menstruation. There is an overdevelopment of the mammary glands and abundant growth of body hair at an early age. In hyperthyroidism the reverse of the above is true, with much dysmenorrhea. This is the eunuchoid type. The ovarian type comes on after menstruation is established. The pains during menstruation are marked and there may be a characteristic pain in the region of the appendix. Ovarian feeding, with hypodermics of pituitrin, gives good results. The pituitary type is more easily diagnosed and if treated early does well on pituitary compounds and other endocrine substances.—Am. J. Obst. & Gynec., 4, 205-206.

Our problems in ENDOCRINOLOGY. Gutman (J.), N. York M. J. [etc.], 1922, 115, 415-418.

A cursory discussion of the present position of endocrinology among the medical sciences.—H. W.

Hypersensitiveness of the skin to x-rays, especially in ENDOCRINE disturbances (Ueber die Röntgen hypersensibilität der Haut, be-

sonders bei innersekretionischen Störungen). Haas (L.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1134-1136.

It was already known that especially in psoriasis, Graves' disease and eczematoid seborrhea there is an increased sensitiveness to x-rays. Haas has found this same irritability in pruritus and secondary chronic lichen simplex. This is probably due to an endocrine dysfunction. Therefore, extreme care is necessary in the dosage of x-rays in treating endocrinopathies.—J. K.

Remarks on the ENDOCRINE system. Hutton (J. H.), Illinois M. J., 1920, 38, 505-509.

The adrenals, pituitary and thyroid, are (to judge by tinctorial reactions) functionally united, forming the chromaffin system. The function of the adrenals is to sustain pulmonary and tissue respiration and they are responsible for the chloasma of pregnancy. Of hyperactivity of the cortex alone the stigmata are overgrowth of hair, and marked muscular development and obesity in males, while a child may attain the size and characteristics of an adult. The anterior lobe of the pituitary has to do with the growth of the skeleton, conditioning dwarfism, gigantism and acromegaly; the development of the genitalia and secondary sex characteristics; the size, shape, and arrangement of the teeth; and the amount and distribution of the hair. The posterior lobe presides over metabolism, carbohydrate tolerance, adiposity, polyuria, and involuntary muscle contraction. Hypothyroidism causes subnormal temperature; cold extremities; myxedematous or dry, doughy, scaly skin; dry, brittle hair and nails; and mental deficiency. Thyroid extract in small doses especially in hypothyroidism results in a rise in temperature, enhanced metabolism, and marked improvement in general nutrition and strength. Thyroid preparations are valuable in diseases due to slowed destruction of toxic wastes, in lowered general nutrition of all tissues, and in all cases in which the process of repair and absorption are deficient—as in delayed union of fracture. The function of the parathyroids is to neutralize toxic substances formed elsewhere in the body. They are concerned with the regulation of metabolism of the guanidin compounds in the body. The thymus and the pineal body are glands which should atrophy at puberty. If they cease functioning before, precocious puberty results; if they persist after, infantilism and sex reversion result. The thymus supplies the excess of phosphorus in organic combination needed for development and growth. It produces nucleins until the bone marrow and the lymphatic glands can take up the work. The thyroid, parathyroids, adrenals, and pituitary have been mentioned as forming the immunizing mechanism of the body. The pituitary, thyroid, and ovaries are closely allied. At the menopause the cessation of the ovarian function is apt to be accompanied by a diminution of function in the thyroid and pituitary. Disorders of the menopause

not relieved by ovarian therapy are benefited by the addition of pituitary and thyroid extract. Vagatonia and sympathicotonia are discussed. Vagatonia is associated with the disturbances of some endocrine gland or glands, especially the thymus and thyroid.

—Author's Abst. (abbreviated).

Some ENDOCRINE aspects of the psyche. Hammar (J. A.), *Folia neuro-biol.* (Leipz.), 1921, 12, 209-230.

A paper which aims to point out that the psychical processes are to some extent dependent on the reaction of the nervous elements to chemical influences, and that the products of the activity of the glands of internal secretion being chemical in nature are known to have an effect upon the nervous reactions of the organism.

—F. S. H.

ENDOCRINES in children. Harper (W. W.), *South. M. J.* (Birmingham), 1922, 15, 536-540.

General review of the pathology of the endocrine glands in children.—F. S. H.

The ENDOCRINES and their relation to future medicine. Holmes (P. K.), *Kentucky M. J.* (Bowling Green), 1922, 20, 567-570.

A general paper pointing out the important relation of the endocrine glands to the future of medicine.—H. W.

Some principles of endocrinology applicable to ORGANOTHERAPY. Hoskins (R. G.), *J. Am. M. Ass.* (Chicago), 1922, 79, 104-106.

Endocrinology, says Hoskins, is, to an unusual degree, an empiric field. Much of the existing confusion in the endocrine field would appear to be due to overanxiety to escape the reproach of empiricism—to force rationalization when no genuine rationalization is possible. It is asserted that endocrinology in some form is going to flourish indefinitely. Parlor endocrinology is even displacing parlor Freudism. For better or for worse, endocrinology has acquired a recognized place in the field of medicine. For two decades practitioners have been avidly seeking enlightenment regarding the practical, everyday problems with which they are confronted. As to how their needs have been met, let the present state of organotherapy testify. So long as the well trained leaders fail to lead, just so long will cheap, commercialized endocrinology have a large following, and medicine be cheapened to the same degree.

—Courtesy Am. M. Ass.

The psyche and the vegetative nervous system with special reference to some ENDOCRINOPATHIES. Jelliffe (S. E.), *N. York M. J.* [etc.], 1922, 115, 382-387.

Primarily the paper is a discussion of the influence of the psyche on endocrine disturbances. The basis of the paper consists of a case history of a young woman who showed signs of mild exophthalmic goiter. A psychoanalysis revealed a deep seated sex complex.—H. W.

ENDOCRINE GLANDS. Nanism and infantilism (*Glandes endocrines. Nanisme et infantilisme*). Lereboullet (M.), *Progrès méd. (Par.)*, 1922, **37**, 233-236.

One of a course of lectures. No new data.—F. S. H.

Changes in the calcium of the blood in otosclerosis and its relation to the **ENDOCRINE ORGANS** (*Blutkalkveränderungen bei Otosklerose und ihre Beziehungen zur Störungen der inneren Sekretion*). Leicher, *Deutsche med. Wchnschr. (Berl.)*, 1922, **48**, 1090.

In 75% of the cases of otosclerosis there was a marked decrease of the amount of calcium in the serum. This low calcium content is due to endocrine disturbances. Hyperfunction of the thyroid, hypophysis and adrenals decreases the quantity of calcium; hypofunction of these organs increases the calcium of the blood. The parathyroids have the opposite influence, while the gonads seem to have no influence.—J. K.

(ENDOCRINE GLANDS) Obesity. The infantile dystrophies and the periglandular syndromes in the child (*L'obésité. Les dystrophies infantiles et les syndromes périglandulaires chez l'enfant*). Lereboullet (M.), *Progrès méd. (Par.)*, 1922, **37**, 285-288.

One of a series of lectures. Generalized discussion.—F. S. H.

(ENDOCRINE) On the structure and development of a fat body or gland in the rat. Long (J. A.), *Anat. Record*, 1922, **23**, 107.

A lobed or branched fat body located in a depression of the muscles between the scapulae is described. It is darker in color than ordinary fat. The contained lipoid is a neutral fat which stains red in Nile-blue-sulphate. It appears in the embryo of 17 days, increases rapidly in size and at birth is relatively large. The whole structure reminds one of an organ of internal secretion such as a corpus luteum.—W. J. A.

(ENDOCRINE) Findings in a case of myotonia dystrophica (*Untersuchungsbefund an einem Fall von Dystrophia myotonica*). Maas (O.) & Zondek (H.), *Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.)*, 1920, **59**, 322.

The case described was somewhat atypical. A significant testicular atrophy was lacking. There was polyuria and pigmentation. The upper arm musculature was atrophic. Response to faradic stimulation was sluggish and delayed. The participation of the

hypophysis, adrenals and thyroid in the final syndrome was evident from the particular landmarks given by the general picture.—F. S. H.

(ENDOCRINE GLANDS) The pathogenesis of deficiency disease.

VIII: The general effects of deficient dietaries on monkeys.

McCarrison (R.), Indian J. M. Research (Calcutta), 1919, 7, 308-345.

The summary of the results of these extensive investigations is as follows. Monkeys fed exclusively on rice, autoclaved at a temperature of 130° for one and a half hours, died on an average within 23.4 days. Monkeys fed on this diet plus butter died in 15 days. The total loss of weight ranged from 25% to 32% of the original weight. The chief clinical evidences were anemia and asthenia, anorexia, diarrhea, weakness of limbs, subnormal temperature and weak cardiac action. Symptoms referable to the nervous system were less prevalent. All classes of deficient dietaries caused an increase in the adrenals and sometimes adrenalin was increased. The weight of the pituitary was also increased by the deficient dietaries. The pituitary was heavier in the females than in the males. Atrophy of the thyroid, reproductive organs, pancreas, spleen and liver occurred.—F. S. H.

ENDOCRINOLOGY: The medical phase. McCaskey (G. W.), Proc. Indiana State M. Ass., 1922, Sept., 28-30.

A large group of cases can be differentiated only by utilizing all the facts concerning endocrinology, and by availing ourselves of the special diagnostic methods which have been developed within the last few years, especially basal metabolism and carbohydrate tolerance. In many cases of endocrine disease there is a perfectly normal basal metabolism. An increase or decrease in carbohydrate tolerance of a given case has an important bearing on diagnostic questions. Frequently the presence or absence of one or two symptoms will point toward the existence of hyperfunction, or hypofunction or dysfunction. It has often happened in my experience that the existence of tuberculosis or endocrine disease as the principal factor in the causation of a given syndrome could be decided in that way. Organotherapy is far from being the only therapeutic deduction derived from a positive diagnosis of endocrine disease. In fact, I feel called on to express a warning, if not a protest, against the indiscriminate exploitation of organic products by commercial interests. In therapeutics, as well as in diagnosis, the endocrine glands have come to the front to stay, but the number of these products that have a proved scientific basis is very small, and their use requires the most painstaking discrimination in order that the patient may not suffer from commercial venders, on the one hand, and unscientific medical practice on the other.

—J. Am. M. Ass., 79, 1545.

INTERNAL SECRETIONS and retarded consolidation of fractures
(*Le secrezioni interne e il ritardo di consolidazione delle frature*).
Marsiglia (G.), Arch. ital. di chir., 1922, 5, 197.

The author sums up previous work on the subject thus: Various researches on different glands all relate to young animals still developing; thyroidectomy, it is agreed, produces some delay in consolidation; thymectomy, not only delay, but actual defect; parathyroidectomy, even partial, according to some, leads to delay, whilst others observe no effect; removal of the suprarenals, unless bilateral and therefore incompatible with life, exerts no influence on repair; oöphorectomy slightly accelerates callus formation. Marsiglia has repeated the experiments on adult dogs, fracturing a leg two or three days after the ablation of the gland, and using controls. Thyroidectomy, partial or complete, causes no delay, though in some cases there seemed to be rather a large mass of callus which was absorbed but slowly; the osteoid phase lasted longer than in the controls. Parathyroidectomy he found technically impracticable. Unilateral suprarenal removal produced no effect; uni- or bi-lateral oöphorectomy had no influence. Complete removal of the pituitary in dogs the author found impracticable by any route, but by the external orbital approach, using a calibrated instrument, he was able to pulp the gland in such fashion that at the post-mortem 40 days later the tissue was found necrotic. Repair of the fractures was unaffected. Histological examination of all the fractures revealed nothing for remark. It is probable, therefore, that there is no one gland, even in man, that has any effect on the course of callus formation, or on the causation of non-union or pseudarthrosis; or that the administration of extracts of one or more of the endocrine glands will have any value, at any rate in the adult.

—Med. Sc., 1922, 6, 383.

(ENDOCRINE) Aids to basal metabolic rate determinations. New-comer (H. S.), Arch. Int. Med. (Chicago), 1922, 29, 748-762.

This paper contains charts and tables so arranged as to facilitate considerably the otherwise laborious calculation of basal metabolism values. (Of technical rather than endocrine interest).—H. L.

Microscopic studies of the ENDOCRINE GLANDS in two cases of ichthyosis (*Récherches microscopiques sur les glandes endocrines dans deux cas d'ichtyose*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. & psychol. de Jassy, 1921, 2, 88-93.

Description given in brief of the histological appearance of the thyroid, parathyroids, hypophysis, adrenals, ovaries and pancreas.

—F. S. H.

(ENDOCRINE) The clinical value of basal metabolism determination. Pickard (R. J.), J. Lab. & Clin. M. (St. Louis), 1922, 7, 669-680.

Case of pigmentation in which no signs of diabetes or cirrhosis were present.—F. S. H.

Of the 150 cases studied 4, or 2.6 per cent, showed signs of endocrine disturbance; one hypothyroidism, two hypopituitary and one ovarian dysfunction. The latter patient, 18 years of age, was sensitive to dog hair. Asthmatic attacks preceded by several days the establishment of menstruation. Treatment with dog hair did not give relief; however, when 5 grains of corpus luteum three times a day were given along with the dog hair she obtained rapid relief and remained free from attacks for 8 months.—H. W.

The author believes that the incretory organs play an important rôle in dental health and disease. His conceptions of endocrine interrelations and therapeutic indications are set forth in elaborate charts.—R. G. H.

A general review.—F. S. H.

Hatai and Hammett (Am. J. Physiol., 1920, 33, 312) have shown that the excitement induced by rough handling causes a modification of the reaction of the rat's intestine to sodium carbonate, and the author has made an investigation of some of the endocrine glands under such excitement, in the hope of locating the cause of the phenomenon. Forty-one pairs of male rats were used; each pair was from the same litter and carefully controlled as to diet. They were stimulated to fight by being placed in a wire cage with a wooden bottom, through which projected the blunt ends of wire nails connected with a battery of dry cells. After from one to six hours the weight, water content, and action of the extracts of the hypophysis, thyroid and adrenals was determined. The results for the thyroid and adrenals were entirely negative. The results for the hypophysis were positive. The gland increased in weight, but

not in water content. The extracts caused contraction of the intestinal strip, while the control caused relaxation, the usual reaction. The modification appeared about one hour after excitation.—T. C. B.

(INTERNAL SECRETIONS) On the influence of visceral extracts, body juices and the dilute solutions of metallic salts on the maintenance of life of the spermatozon. Uramato (S.), Jap. Med. World (Tokyo), 1921, 1, 18. Author's abstract from Nisshin Igaku, 1921, 10, No. 8.

Cerebrospinal fluid, aqueous humor and uterine extract of the rabbit, extracts of the liver, testicles and lymphatic glands of the albino rat are more adapted for the preservation of the life functions of the spermatazoa of albino rats which have been taken out of the body than is physiological salt solution. The preservation of the life of the spermatazoa of albino rats in the extracts of the brain, hypophysis, seminal vesicle, prostate, adrenal capsule, salivary glands, spleen, lung uterus and vagina, ovaries and fallopian tubes of albino rats and the peritoneal juice of the rabbit are as effective as is physiological salt solution. The bile of the rabbit, the serum of rabbit and rat, the lymph of the rabbit, the extracts of the stomach, intestines and the muscles of albino rats are inferior.
—F. S. H.

Importance of INTERNAL SECRETIONS in etiology of impetigo herpetiformis. Walter (F.), Ploska Gaz. Lekarska (Cracow, Lodz, Lwow, Vilna, Warsaw), 1922, 1, 425-427.

Reference cited from J. Am. M. Ass., 70, 1188.

The GASTRIN theory put to physiological test. Ivy (A. C.) & Whitlow (J. E.), Am. J. Physiol. (Balt.), 1922, 60, 578-588.

A "two gastric pouch" was made in order to test the "gastrin theory" which maintains that substances in contact with the mucosa of the pyloric antrum cause the formation of gastrin which is absorbed and stimulates the glands of the fundic mucosa. The authors failed to obtain an increase of secretion in the Pawlow pouch when various substances were applied to the mucosa of the pyloric pouch. The work of Edkins and Tweedy was repeated, and demonstrated an inadequate control of their experiments.—T. C. B.

(GONADS) An atypical formation from the follicular elements in an OVARY transplanted into the dog (Sur une formation atypique constituée aux dépens des éléments folliculaires dans un ovaire transplanté chez la chienne). Athias (M.), Compt. rend. l'Ass. d. anat. (Par.), 1921, May, 21-23.

An autotransplanted ovary enlarged considerably. On removal at autopsy numerous cysts were found. The genital tract was normally developed. Histological study of the implant showed ova in

various stages of development. A peculiar cellular arrangement in connection with one of the follicles is described.—F. S. H.

(GONADS) Effects of castration on the automaticity of the uterus of the guinea-pig (*Effets de la castration sur les mouvements automatiques de l'utérus chez le cobaye*). Athias (M.), *J. de Physiol. et de path. gén. (Par.)*, 1919, **18**, 731-743.

The uterine muscle possesses both clonic and tonic functions. When guinea-pigs are castrated the motility of the uterus is markedly modified in that there is a gradual weakening of the intensity of the automatic contractions up to the point of their complete cessation while the tonic function remains, and even at times appears to be a bit enhanced. These changes are attributed to the suppression of the internal secretion of the ovary. They are not found in animals in which ovarian implants have been made after ovariectomy.—F. S. H.

(GONADS) The interstitial cells of the OVARY of Cheiroptera (*Récherches sur les cellules interstitielles de l'ovaire des Chiroptères*). Athias (M.), *Arch. de Biol.*, 1919, **30**, 89-212.

An extensive histological study with bibliography. The interstitial cells reach their maximum development during the periods of pregnancy and lactation. In the autumn a regression occurs, while towards the middle of the winter an increase begins. The interstitial cells resemble those of other mammals and show the characters of glandular elements. In young animals the source of the cells is largely the connective tissue of the ovarian stroma. Later the theca interna of the atretic follicles is the principal source.
—F. S. H.

(GONADS) Two cases of INFANTILISM with mental infirmities (*Deux cas d'infantilisme avec infirmités mentales*). Ballif (L.), *Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy*, 1921, **2**, 57-66.

Ballif is inclined towards the pluriglandular hypothesis of the etiology of infantilism. The cases, which present no unusual features, are described, but record of treatment is not given.—F. S. H.

(GONADS) Case of essential gynecomastia (*Un cas de gynecomastie essentielle*). Ballif (L.), *Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy*, 1921, **2**, 158-160.

The right breast was enlarged. Testicular traumatism or genital infection was not reported and there was no pain.—F. S. H.

(GONADS) The production of liquid of the seminal vesicles in relation to the internal secretion of the TESTICLES (*La production du liquide des vésicules séminales en rapport avec la sécrétion*

interne des testicules). Battelli (F.) & Martin (J.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 429-431.

The development and the secretory functions of the vesiculæ seminales are dependent upon the internal secretion of the testicles. Castration causes atrophy of the vesiculæ with cessation of the vesicular liquid. We can thus observe the quantities of liquid produced in a given time, and follow the modifications of the hormonal activity of the testicles. We can obtain a complete ejaculation at will by the method of Battelli. In order to have comparable results, all the guinea pigs were subjected to one ejaculation a week, made under the same conditions. Individual differences are considerable. There are variations with the season, the quantity of vesicular fluid being greatest in the spring. There is no notable difference due to temperature. Frequency of ejaculation and ligation of the vas deferens cause diminution of the vesicular fluid. Injection of testicular extracts is without effect in restoring the secretion.—T. C. B.

(GONADS) Ovarian transplantation (À propos des greffes ovariennes). Bazy (P.), *Bull. Acad. de méd. (Par.)*, 1921, **86**, 106; abst., *Rev. franç. de gynéc. et d'obst. (Par.)*, 1922, **17**, 41.

In discussing the report of Tuffier (q. v.), Bazy expresses skepticism as to the value of ovarian grafting. The results of Tuffier, he states, are only temporary when they are not absolutely nil. Opothrapy will accomplish just as much in preventing ablation symptoms.—E. N.

(GONADS) A case of androgynous pseudo-hermaphroditism with an intra-abdominal tumour following the removal of a rudimentary genital gland. Rapid disappearance of this tumour under radiotherapy (Un cas de pseudo-hermaphroditisme androgyne avec tumeur intra-abdominale consécutive à l'ablation d'un rudiment de glande génitale. Disparition rapide de cette tumeur sous l'influence de la radiothérapie). Béclère & Siredey, *J. de radiol. et d'électrol. (Par.)*, 1921, **5**, 211.

The authors describe the clinical features of a case of a woman of 54, who had an abdominal tumour which appeared to be a large bossy tumour of the spleen. Some points about the case resembled that of a porter seen nine years previously by Béclère, in which the tumour followed on the removal of a neoplasm of the left testicle. Two important facts were observed in the present case. (1) A cystic tumour had been removed from the left inguinal region four years previously. (2) The patient had never menstruated. From a clinical examination it appeared that the case was one of androgynous pseudo-hermaphroditism; the external genital organs and the breasts were female in type, and a small mass under the skin at the upper part of the right labium magus immediately below the external

inguinal ring was looked upon as a rudimentary testicle. The cystic tumour previously removed from the left side had not been microscoped, but a description by the surgeon strengthened the belief that the mass on the right side was a rudimentary testicle. The inguinal tumour and the large splenic tumour were regarded as cause and effect, and, since operation was refused, radiotherapy was the only available treatment; treatment lasted about five months and comprised twenty séances, weekly at first and then at longer intervals. A description is given of the method of applying the rays. The results obtained were very good and rapid; ten days after the first séance the tumour was distinctly smaller and the pain caused by it considerably less. Six weeks from the beginning of treatment radiosopic examination of the abdomen showed nothing abnormal; a month later the patient had no pain and the spleen was palpated with difficulty. Irradiation was continued as a precaution against recurrence. Later the patient put on weight, but she complained that brain-work was more difficult and tiring than formerly. The latter part of the paper is taken up by an account of the case treated some years previously by Béchère.—Med. Sc., 5, 546-547.

(GONADS) The energy requirements of girls from 12 to 17 years of age. Benedict (F. G.) & Hendry (M. F.), Boston M. & S. J., 1921, 184, 217-222; 257-262; 282-286; 297-306; 329-334.

Basal metabolism was studied in a group of girls ranging from 13 to 17 years of age. No influence of puberty or the prepubescent stage was clearly proved in any of the results.—H. W.

(GONADS) An apparently hopeless case of polyglandular disturbance with infantile genitalia in a boy of 17½ years: complete cure at 21 years. Boynton (C. E.), South. M. J. (Birmingham), 1922, 15, 619-620.

Case report. The patient showed delayed sexual development, with general body form of the female type. The psyche was that of a normal boy. The only glandular defect noted was an underdevelopment of both testes, which were in their normal position. Treatment by feeding extracts of pituitary, thyroid and thymus, as well as "didymin," at different times had no effect. The case yielded to mechanical treatment.—J. C. D.

(GONADS) After results of removal of uterine appendages in hysterectomy for uterine fibroids and chronic metritis. Bride (J. W.), J. Obst. & Gynæc. Brit. Emp. (Lond.), 1922, 29, 68-87.

As a result of a questionnaire study of 231 patients, Bride arrives at the following conclusions. The general health of nearly all the patients after both operations is much better, but a larger percentage are better after the radical operation. The temperature of the patients is adversely affected in only a small percentage after

either operation, but after the conservative procedure this percentage is slightly larger. Flushings occur in a large percentage of patients after either operation. The percentage is slightly greater after the radical operation. A very small percentage of patients complain of nervous symptoms after operation, but the percentage is larger after the conservative operation. A very small percentage of women after either operation complain of more pain, but after the conservative operation it is more than twice the percentage of that after the radical operation. A larger percentage of women have disturbances of their sexual relations after the radical than after the conservative operation in the proportion of 39 to 26 per cent. There is a greater tendency to adiposity when both ovaries are removed. In brief, then, so far as the majority of the manifestations of the artificial menopause are concerned, there is very little to choose between the two types of operation. The advantage lies with the radical operation in every way save two. The two exceptions are the occurrence of flushes and the sexual disability.

—E. N.

(GONADS) The changes in the white cell picture of the blood during the MENSTRUAL cycle (Ueber das Verhalten des weissen Blutbildes während des menstruellen Zyklus). Caminer (L.), Zentralbl. f. Gynäk. (Leipz.), 1921, 45, 1601-1604.

The changes in white cell relationships in the normal menstruating woman follow a certain course specific for the individual although the relation of the white cell picture and ovarian activity during the menstrual cycle shows no general regularity. In amenorrhea the variations in white cells are greater than in menstruation, the total leucocytes are low, and the general relationships are not altered when ovarian substance is fed.—F. S. H.

(GONADS) Delayed hereditary lues: endocrinopathies, dystrophias in man of genital origin (Lues hereditaria tardia: endocrinopatias, distrofias de origen genital en el hombre). Castex (M. R.) & Waldorp (C. P.), Prensa méd. argentina (Buenos Aires), 1921, 7, No. 30.

A clinical and pathological case report. The author attributes the infantilism to hereditary syphilis stimulated to activity by anhylostomiatic toxines.—B. A. H.

(GONADS) Operative attempts at organic rejuvenescence and the therapeutics of genital gland dystrophy (Os ensaios operatorios de rejuvenescimento orgânico e a terapeutica da dystrophia genitoglandular). Castro (A. de), An. Fac. de Méd. (Montevideo, Uruguay), 1921, 6, 233-244.

Brief descriptions are given of 3 cases of genital dystrophy in which evidences of hypophyseal enlargement were absent. A good review of the operation and principles of Steinach is given.—F. S. H.

Inoculation of vaccinal pulp into the TESTICLE of the rabbit (Sur l'inoculation de pulpe vaccinale dans le testicule du lapin). Condrea (P.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 895-896.

Not of endocrine interest.—T. C. B.

(GONADS) Climacteric hypertension. Cummings (R.), Calif. State J. M. (San Fran.), 1921, 19, 116-119.

The author concludes from a study of 158 women in whom the systolic blood pressure was greater than 160 mm. that there are a few cases in which an endocrine disturbance is the possible and entire cause of the hypertension. There are a great number, however, in whom this disturbance is only a minor factor; other factors, such as foci of infection, chronic constipation, fatigue, thyroidism and nephritis are the great factors in the etiology. The administration of thyroid and corpus luteum extracts give excellent results in those cases of hypertension due to an endocrine disturbance; however, their unaided use is of no particular avail in those with hypertension from other causes.—H. W.

(GONADS) Vasomotor reactions of the penis. Crawford (A. C.) & George (J. M.), J. Urol. (Balt.), 1921, 5, 89-118.

Plethysmographic curves of the penis and of the hind leg were taken in the dog. The penis volume was increased by drugs which caused limb dilatation, and also by orchitis extract.

—Physiol. Abst., 6, 276.

(GONADS) Dysovaire. Dalché (P.), Gynécologie (Par.), 1922, 21, 385-420.

Dysovarianism is a disturbance of the ovarian function. A massive review of the various manifestations of the disorders emanating from such conditions is given.—F. S. H.

(GONADS) Reversible secondary sex phenomena. Draper (G.), Med. Clin. N. Am. (Phila.), 1921, 4, 1345-1374.

A generalized presentation of 3 male and 2 female patients exhibiting reversible secondary sex phenomena. No attempt has been made to elaborate hypothetical explanations. The cases are offered as typical examples of those endocrinopathic states which are perhaps most definitely established.—F. S. H.

(GONADS) On the relations between fertility and nutrition. II. The OVULATION rhythm in the rat on inadequate nutritional regimes. Evans (H. M.) & Bishop (K. S.), J. Metab. Research (Morristown), 1922, 1, 335-356.

The effects of defective nutrition are summarized. A standard diet, consisting of whole wheat 67.5, casein 15, whole milk powder 10, sodium chloride 1, calcium carbonate 1.5 and butterfat 5 parts

been reported in cladocera, crustacia, birds and cattle. Cattle often deliver themselves of twins. It frequently happens that the female co-twin, the other being a male, is usually sterile and has a modified genital tract, thus resembling the human pseudohermaphrodite. These animals are known as free martins and their gonads as free martin gonads. The structure of the latter may be any degree of transformation of the ovary into the testis, as a result of the hormone action of the testis of the male co-twin. Atypical gonad development in the human pseudohermaphrodite cannot be explained on the basis of the hormone action of a male co-twin, but knowing that sex determination is transmitted through the primary germ cell, is it not possible that this sex determination for some unknown reason is perverted, and that this perversion is inherited? The author describes a case of pseudohermaphroditismus feminus externus with a gonad in the right labium which he presumes was a rudimentary testis, possibly to be classed as similar to a free martin gonad of cattle. (It was not removed.) The uterus, tubes and ovaries were apparently absent.—E. N.

(GONADS) The falsetto voice in the male—with a demonstration of four cured cases. Green (J. S.), *Laryngoscope* (St. Louis), 1921, 31, 33-41.

Voice in childhood is essentially the same in both sexes. The larynx develops but little between the age of 5 years and puberty; however, in boys there is a gradual increase in the pectoral tones. After puberty is reached, concomitant with general system changes, pronounced changes of larynx and voice takes place. In boys the larynx shows rapid growth, especially in the transverse diameter. In girls the growth is mainly vertical, the larynx remains small, delicate and highly nervous. Growth of the larynx is accompanied by enlargement of the glottis. The position of the larynx is a little higher in women than in men. Falsetto voices are found in both sexes after sex maturity. The term "eunuchoid voice" has been used as synonymous with that of falsetto voice. This interchange of phrases is to be deplored for the reason that a falsetto voice may occur in a person fully developed sexually. In practically all cases a falsetto voice is the result of a faulty habit contracted at the time the voice is changing and retained in later life.—H. W.

(GONADS) Oxytocic substances in the PLACENTA [Die Wehen-substanzen in der Placenta (Erwiderung auf den Artikel: Organ-extrakte als Wehenmittel)]. Guggisberg (H.), *Monatschr. f. Geburtsh. u. Gynaek.* (Berl.), 1921, 54, 277-279.

Guggisberg finds that extracts of all the glands of internal secretion have a stimulatory action upon the uterine muscle, but that this action is most pronounced in extracts of the thyroid and placenta (the pituitary gland being excepted). The activity of the

extracts is referred to a proteinogenic amine. The fluid obtained from the placenta by the Buchner process is free from lipid and protein and is not poisonous for man or for rabbits. From clinical experimental work, it was found that the extract has the most pronounced effect during the first stage of labor. When it is administered in conjunction with pituitary extract, the effect is more marked. Pituitrin works best during the second stage and it is conceivable that this is due to the mobilization during the first stage of some material, which makes the uterine muscle more susceptible to the action of pituitrin. Clinically the writer uses simultaneous injections of the two extracts (placenta and pituitary), especially during the first stage, when pituitrin alone is of little avail. Shortly after the injection the pains, which were weak and infrequent previously, become stronger and longer, while the interval is shortened. The effect of the extracts continues for a surprisingly long time. Failures were very few and there were no untoward effects on the child. The combination also works well in the second stage, but little stress is placed on this action, because it is difficult to determine what part the placental extract plays, since the pituitrin alone is so efficient.—*Am. J. Obst. & Gynec.*, 1922, 4, 206.

(GONADS) Bidder's organ and the secondary sex characters in the toad (*Bufo vulgaris* Laur) [*L'organe de Bidder et les caractères sexuels du crapaud (Bufo vulgaris* Laur)]. Guyénot (E.) & Ponce (K.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 751-752.

Recently Harms has reported that the secondary sex characters in the toad are dependent in part on Bidder's organ. From experimental evidence the authors arrive at an exactly opposite conclusion. After ablation of Bidder's organ there is development of the digital excrescences, mating, clasping reflex very clear, and living descendants. The excrescences are identical with the controls. After ablation of the testicles there are no digital excrescences, no sexual attraction, no clasping reflex. The same is true for ablation of both Bidder's organ and the testicles. It is concluded that the secondary sex characters in the toad, as in general, are dependent on the testicles and not on Bidder's organ. The latter is perhaps a rudimentary organ, bearing the same relation to the gonads that the pronephros bears to the unesonephros.—T. C. B.

(GONADS) Anatomico-clinical observations of the relation between the evolution of the CORPORA LUTEA and the appearance of menstruation (23 observations) [*Recherches anatomico-cliniques sur les rapports entre l'évolution du corps jaune et l'apparition des règles (23 observations)*]. Henry (J. R.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1162-1164.

Examination of the ovaries removed from 23 women at varying phases of their menstrual cycle leads to the conclusion that there is no chronological relation between the development of the corpus

luteum and the appearance of menstruation. They vary greatly according to the subject and under the influence of causes that cannot be fixed. There are women menstruating regularly in whom no corpora lutea in evolution can be discovered.—T. C. B.

(GONADS) Specific OVARIAN secretion (Ueber das spezifische Ovarialsekret). Herrmann (E.), Zentralbl. f. Gynäk. (Leipz.), 1921, 45, 501.

Polemical against Fellner.—F. S. H.

(GONADS) Some moot points in the diagnosis of the causes and in the treatment of sterility. Hirst (B. C.), Am. J. Obst. & Gynec. (St. Louis), 1922, 4, 160-165.

Of no endocrine interest except in emphasizing the importance of the rôle of "lack of genital sense," and also of adiposity.—E. N.

(GONADS) Increased blood sugar coincident with OVULATION in pigeons. Honeywell (H. E.) & Riddle (O.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 377-380.

The results indicate that the stage with reference to ovulation is probably a factor influencing the values obtained for blood sugar of other animals and is probably too large a factor to be left out of consideration in dealing with samples taken from reproducing females. The essential similarity of the curve expressing the rise of the blood sugar with the curve expressing the coincident hypertrophy of the adrenals is evidence of a relation of the latter to carbohydrate metabolism and to sexual function. The enforcement of ovulation throughout the year is accompanied by an increased carbohydrate mobilization.—F. S. H.

(GONADS) On an OVARIAN neoplasm of the follicular type (Sur une néoplasie ovarienne offrant des dispositions de type folliculaire). Lagarde (R.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1159.

Morphological.—T. C. B.

(GONADS) Development of interstitial glands (Zur Entwicklung der interstitiellen Geschlechtsdrüse). Lahm (W.), Monatschr. f. Geburtsh. u. Gynäk. (Berl.), 1922, 58, 128-141.

See Endocrin., 6, 701.

(GONADS) X-ray versus surgery in the treatment of fibroid tumor of the uterus. Lane (J. L.), Northwest Med. (Seattle), 1922, 21, 241-243.

The author points out some of the advantages of x-ray therapy as compared with surgery in fibroids of the uterus. Amenorrhea is produced, and thus the most dangerous symptom, hemorrhage, is pre-

vented. The x-ray menopause he finds somewhat milder than that following surgical castration, and if the dose can be graduated to destroy the ovarian follicles but leave the interstitial tissue intact, the endocrine effect of the ovary would not be destroyed and the after symptoms mild if at all present. Other factors such as mortality and expense are mentioned.—H. L.

(GONADS) An early stage of the free-martin and the parallel history of the interstitial cells. Lillie (F. R.) & Bascom (K. F.), Science (N. Y.), 1922, n. s. 55, 624-625.

The theory that the intersexual condition of the free-martin depends upon hormones secreted by interstitial cells of the testis of the male twin has presumed that the male hormone is effective shortly after the beginning of sex-differentiation in the embryo. The earliest stage of the free-martin hitherto described is 7.5 cm. The gonads of a 3.75 cm. free-martin are described as being much less than half the bulk of those of normal males and females of a corresponding age. The cortex of the ovary is only about one-fifth the thickness of that of the normal female of corresponding age. The following conclusions are drawn. The appearance of interstitial cells in the testis at the very time that a male hormone may be demonstrated by its physiological effects (free-martin) is strong evidence that these cells secrete the sex hormone. The absence of such cells in the female and the corresponding lack of effect of the female blood on the male twin argue in the same sense. In the female of cattle sex-differentiation before birth is apparently due to genetic factors exclusively; in the male the genetic factors are intensified by the production of a hormone.

(GONADS) On the internal secretion of the sexual glands. Lipschütz (A.), J. Physiol. (Lond.), 1917, 51, 283-286.

Reviewing briefly the known experimental data on the question, Lipschütz describes the external genitalia of a female guinea-pig into which testes had been implanted. He concludes that the testis has evoked a transformation of the clitoris into a penis-like organ. Moreover the body temperature of the feminized males corresponds to that of the normal female. It is therefore concluded that the puberty glands of the female tend to increase the body temperature.—F. S. H.

(GONADS) Hypertrophy of OVARIAN fragments (Nouvelles observations sur l'hypertrophie des fragments ovariens). Lipschütz (A.) & Wagner (C.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1122-1123.

In making a laparotomy on a female rabbit that had been castrated 18 months before, it was noticed that the uterus was more developed than in the normal controls from the same litter. Two

ovarian fragments were found near the uterus, left behind at the time of operation. The ovules were reduced in number but the follicles were not. This reaction of the uterus, so sensitive to variations in the endocrine function of the ovaries, was due to the fragments, and the internal secretion of the ovary was due to the number of cells derived from the follicular development of the ovules, rather than from the number of ovules themselves.—T. C. B.

(GONADS) Is the hypertrophy of the interstitial cells of the TESTICLE a compensatory endocrine reaction (*L'hypertrophie des cellules interstitielles du testicule est-elle une réaction compensatrice endocrine*)? Lipschütz (A.) & Wagner (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 15-17.

Further evidence in support of their contention that the hypertrophy of the interstitial tissue in testicular fragments is not a compensatory endocrine reaction.—T. C. B.

(GONADS) Hypertrophy of the TESTICLE in unilateral castration (*Sur l'hypertrophie du testicule dans la castration unilatérale*). Lipschütz (A.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 60-62.

Affirmation of the thesis that the greater weight of the remaining testicle after unilateral castration is due to an acceleration of development, and that hypertrophy does not take place.—T. C. B.

(GONADS) The minimal quantity of the TESTICULAR mass sufficient for complete masculinization (*Nouvelles observations sur la quantité minimale de masse testiculaire suffisante pour une masculinisation complète*). Lipschütz (A.), Wagner (C.) & Kropman (E.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 122-124.

An answer to their critics with new observations on a guinea-pig and two white mice. Contains no novel additions to present knowledge.—T. C. B.

(GONADS) The influence of the internal secretions of the TESTIS on blood pressure (*Über die Wirkungen des inneren Sekrets der Keimdrüsen auf den Blutdruck*). Loewenthal (M.), *Klin-therap. Wchnschr. (Wien & Berl.)*, 1921, **28**, 355-361.

The internal secretion of the testis produces changes of blood pressure only indirectly by increasing the tone of the sympathetic system. Ovarian secretion increases vagus tone, and also produces local vaso-dilatation.—*Physiol. Abst.*, **7**, 315.

(GONADS) The flies on the chariot wheel. Lydston (G. F.), Illinois M. J. (Oak Park), 1922, **42**, 97-101.

A discussion, in a series of categorical statements, of the virtue of giving credit to whom credit is due. Lydston claims priority in being the first surgeon successfully to transplant a testicle from one

human being into another, the first to transplant a testicle from a dead human being to a living human being (Lydston himself being the recipient), and the first successfully to transplant an ovary from a dead woman to a living woman. The author states that writers on this subject are prone to omit mention of his name as one who has done pioneer work in this field.—I. B.

(GONADS) The OVUM as an internal secretory organ. McIlroy (A. L.), N. York M. J. [etc.], 1922, 115, 404-406.

A short paper of rather theoretical interest pertaining to the ovum as an incretory organ.—H. W.

(GONADS) The male sexual glands in the prevention of creatinuria. McNeal (M. D.), Am. J. M. Sc. (Phila.), 1922, 164, 222-227.

Data are presented regarding two eunuchs, three men with a congenital testicular defect, and one man with a defect acquired at the age of 27. The men who were castrated at the ages of 29 and 47, respectively, excreted creatin. Analysis of the urine of the three men with congenital defects, and one with a deficiency acquired at the age of 31, showed the presence of creatin regularly. Besides the sexual incompetence on an organic basis in one of the congenital defects a diagnosis of diabetes insipidus was made—J. F.

(GONADS) Can Steinach's operation produce rejuvenation of the animal organism (*L'opération de Steinach peut-elle realizer le rajeunissement de l'organisme animal*)? Marinesco (M. G.), Bull. gén. de therap. [etc.] (Par.), 1922, 173, 335-368; Presse méd. (Par.), 30, 309-311.

A review and a discussion best summed up in the quotation: "If Steinach had been better acquainted with the histological and physico-chemical processes which characterize senility, or even the non-reversibility of biological phenomena in general, he quite probably would have hesitated before speaking of rejuvenation."

—F. S. H.

(GONADS) "PLACENTA-OPTON" as oxytocic (*Placenta-Opton als Wehenmittel*). Martin (E.), Monatschr. f. Geburtsch. u. Gynaek. (Berl.), 1921, 54, 288-291.

To test the efficacy of Merck's Placenta-Opton, Martin selected 6 patients, in whom the membranes had ruptured before the onset of labor. After several hours' observation, in each patient with the pains absent or very weak and irregular, an ampoule of the Placenta-Opton was injected intramuscularly. Within a few minutes after the administration of the drug, contractions become more severe and recurred at closer intervals. In no case was there any apparent harmful effect on mother or child. He was not able to start pains in patients who gave no signs of being in labor, but is quite con-

vinced that rhythmic uterine contractions can be induced by the substance when the patient is at term.

—Am. J. Obst. & Gynec., 4, 207.

(GONADS) Non-teratoid tumors of the OVARY (*Essai sur les tumeurs non teratoides de l'ovaire*). Masson (M. P.), Gynéc. et Obst. Rev. (Par.), 1922, 6, 81-105.

A histo-pathological study.—F. S. H.

GONADS) Brief considerations of the secretion of the mammary glands from the point of view of therapeutics (*Breves consideraciones sobre la secreción mamaria desde el punto de vista terapéutico*). Montaña (A.), Observador Med. (Mexico), 1920, 1, 174-181.

Report of one case in which the injection of homologous milk facilitated the function of lactation.—F. S. H.

(GONADS) The formation and function of the CORPUS LUTEUM (*Zur Frage der Bildung und Funktion des Corpus luteum*). Novak (J.), Zentralbl. f. Gynäk. (Leipz.), 1921, 45, 960-962.

Controversial with Sieber. Nothing new.—F. S. H.

(GONADS) Arterial hypertension following castration in women (*L'hypertension artérielle consécutive à la castration chez la femme*). Paillard (H.), J. méd. franç. (Par.), 1921, November; abst., Rev. franç. de gynéc. et d'obst. (Par.), 1922, 17, 65.

Among 25 women with hypertension were 14 in whom the menopause had been produced (12 by operation, 2 by radiotherapy). Conversely, of 31 castrated women, 13 presented a tendency to, and 3 a definite hypertension. The author explains this hypertension on the basis of work showing that ovarian extracts cause hypertension, being thus antagonistic to the adrenals. Castration causes adrenal hypertrophy, this, in turn, being responsible for the hypertension, according to the author.—E. N.

(GONADS) Sobre etiología del glaucoma. Paltracca (E.), Gior. di Ocul., Nov. 11, 1921; abst., Rev. Sud-Am. (Buenos Aires), 1922, 5, 229.

Glaucoma, more frequent in women than men, is observed in those who have passed 60 years of age. The author believes in the possibility that the origin is endocrine. Ovarian as well as testicular extract diminishes the ocular tension in those subjects who for some time have been at the critical age or period, but in the young normal individual it is without effect. In glaucoma the extract causes the endobulbar tension in the unaffected eye to diminish a great deal, but it exerts scarcely any action upon the glauco-

matous eye. If by iridectomy the glaucomatous eye is restored to normal tension ophotherapy will maintain it so.—W. H.

Case of premenstrual psychosis (*Sur un cas de psychose menstruelle*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 53-57.

Not suitable for abstracting.—F. S. H.

(GONADS) Action of cerebral and OVARIAN lipoids in epilepsy (*Action de lipoides cérébraux et ovariens dans l'épilepsie*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 63-65.

The effect of the intravenous injection of cerebral lipoids was negative. The same obtained in the one case tried with ovarian lipoids.—F. S. H.

(GONADS) ORCHITIC lipoids in epilepsy (*Action des lipoides orchitiques dans l'épilepsie*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 65-68.

Parhon feels from observations on five patients that the administration of orchitic lipoids reduces the number of epileptic attacks.
—F. S. H.

(GONADS) Case of Dercum's disease (*Sur un cas de syndrome de Dercum*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 66-70.

A case of adiposis dolorosa occurring at the menopause. Parhon believes that the disorder is pluriglandular and in part attributable to disturbance in the genital gland functions, particularly an insufficiency.—F. S. H.

The glycogen content of liver and muscles in castrated animals (*Sur la teneur en glycogène du foie et des muscles chez les animaux châtrés*). Parhon (M.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 741-743.

The quantity of glycogen in liver and muscles depends on the time at which the animals are sacrificed after castration. Six weeks after castration there is a slight diminution of hepatic glycogen, but no appreciable difference in the muscles. If, however, the animals are allowed to live a year, there is a marked diminution in the liver and muscle glycogen. It is suggested that this is due to a disturbance of other endocrine glands, the result of the castration.—T. C. B.

(GONADS) Significance and origin in OVARIAN tumors of certain arrangements recalling those of a cylindroma (*Signification et origine dans les tumeurs de l'ovaire de certaines dispositions rappelant celles du cylindre*). Peyron (A.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1156-1159.

Morphological.—T. C. B.

(GONADS) Therapeutic use of PLACENTAL extracts (Die Therapeutische Verwertung der Placenta). Puppel (E.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1921, 54, 280-288.

Puppel employed a 5 per cent solution of Merck's "Placenta-Opton" and gave the preparation intramuscularly but never intravenously. After a limited experience he draws the following conclusions. Placenta-Opton can be used therapeutically to increase the severity of the pains in any stage of labor. The intramuscular injection of this substance has a good effect upon all menstrual disorders due to hypofunction of the uterus.

—Am. J. Obst. & Gynec., 4, 206-207.

(GONADS) New investigations on the biology of the OVARY (Nuevas investigaciones acerca de la biología del ovario). Ramirez (E.) & Ochoterena (I.), Rev. Mex. de biol., 1920, 1, 88-107.

Histological studies of the ovary during the various stages of menstruation or heat in animals. From the observations made, the authors are of the opinion that the secretion of the corpus luteum produces the necessary modification of the uterine mucosa essential for nidation. If fecundation occurs there is a transformation into the corpus luteum of pregnancy which has a special function. There is an antagonistic action existing between the corpus luteum and the interstitial cells. When the former recedes the secretory action of the latter becomes manifest. The secretion of the interstitial cells is considered as the determinative cause of menstruation for during this period the action of the corpus luteum ceases while the interstitial cells yield a picture of intense activity. The ovarian congestion of menstruation favors ripening of the ovum, which in turn impedes corpus luteum development.—F. S. H.

(GONADS) Local and general effects due to the resection of the vas deferens (Effets locaux et généraux dus à la résection des canaux deferents). Retterer (E.) & Voronoff (S.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1073-1075.

A histological explanation of the preservation of sexual ardor and power after resection of the vas deferens.—T. C. B.

(GONADS) Vasectomy on the dog as regeneration experiment (Vasektomie beim Hunde als Regenerationsexperiment). Sand (K.), Monatschr. f. Sexualwissenschaft. (Berl.), 1922, 8, 3-8.

Report of the beneficial effects of vasectomy on one old dog. —F. S. H.

(S) Experimental hermaphroditism (De l'hermaphroditisme expérimental). Sand (K.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1017-1024.

tract causes transplantation and inversion show that we can utilize a great deal, uncombined hormones, and we are led to ask if it is

not possible to use the combined influence of the male and female gonads, and thus produce hermaphrodites. The author experimented on a young castrated male guinea pig. Transplantation of an ovary was made in the right abdominal wall, and a testicle on the left side. The combined influence of the two glands was shown by the development of the penis and by the development of the mammary glands, which secreted milk and were histologically of the puerperal type. *Psycho-sexually the animal was often bi-sexual, passing in the course of an hour from a placid female to a violent male when put near a male, or a female, or a new born animal.* The technique of Sand's method of intratesticular implantation of the ovary is given and the results of experiments described. Of 10 infantile guinea pigs thus operated upon, 2 developed positive hermaphroditism; the penis was normal compared to the controls, but, whereas in the controls the nipples were very small, in the operated animals the mammae were turgescent and secreted an abundance of milk. Of 6 guinea pigs operated upon at puberty, 2 gave successful results. The results in animals of an advanced age are not clear. The histology of the ovario-testicles is given. The work is published in extenso in the "J. de Physiol. et de path. gén."—T. C. B.

(GONADS) Formation and function of the CORPUS LUTEUM (Zur Frage der Bildung und Funktion des Corpus luteum). Sieber (H.), Zentralbl. f. Gynäk. (Leipz.), 1921, 45, 332-340.

No new data.—F. S. H.

(GONADS) Some aspects of sterility. Solomons (B.), Irish J. M. Sc. (Dublin), 1922, 5s, 303-313.

In dealing with sterility from constitutional causes the glands of internal secretion must in these days present themselves *pari passu*, at any rate, with other causes. They are all important and most important of all is the corpus luteum. For a patient who has scanty menstruation, or none, the result following the administration of corpus luteum is in some cases nothing short of miraculous. In one case, where the patient had never menstruated, the drug apparently started menstruation, six months after which pregnancy occurred. This patient did not nurse her child and menstruation did not return. After two years she wrote expressing her impatience at the absence of pregnancy. Corpus luteum was again recommended, menstruation returned for two months, after which she again became pregnant. The dose recommended is 5 grains daily for two days, then gradually increasing the amount until at the end of another month 10 grains three times daily are being taken. Anaphylaxis has never been noticed. The great disadvantage of the treatment is the expense, especially for dispensary patients. Parke Davis capsules of corpus luteum have been ordered always. The best results have been obtained with corpus luteum. Whole ovarian gland has also been used very successfully, both by mouth and

portal regions of the liver lobules. Extracts of the placenta and other organs proved to be non-toxic. It was found that the blood of a pregnant woman or that of a woman during the menstrual period destroyed the new extract of corpus luteum, whereas the blood of non-pregnant women and that of men did not have such an effect, the toxicity not being destroyed. This is, therefore, suggested as a test for pregnancy. The change produced in the toxic substance by the serum is detected by the refractometer. Simultaneous injection of cholesterol greatly modifies the toxic effects. The authors, therefore, conclude from their few experiments that eclampsia is due to hyperactivity of the corpus luteum of pregnancy. That hypercholestinemia of pregnancy is most marked in eclampsia, is cited as supporting this view.—I. M.

(HYPOPHYSIS) La HIPOFISIS, estudio clinico-terapéutico. Alou (P.), Union méd. Espania, Jan. 7, 1922; abst., Rev. Sud-Am. (Buenos Aires), 1922, 5, 228.

Alou employs the injectable hypophyseal extracts and "hypophysina" with very satisfactory results in the following pathological states: in exophthalmic goiter, in which he obtains diminution of the volume and weight of the gland; in adrenal insufficiency, in which it provokes hypertrophy of the gland; usually in epilepsy; in acute myocarditis of toxic-infectious processes; in myocarditis and cardiac valvular insufficiency, except the aortic with hypertension, alternating its use with digitalis; in the menopause, accompanied by affections of the ovary; in all those asthenic conditions, gastric myasthenia, convalescence from infectious diseases; in essential diabetes insipidus and urinary incontinence; in inertia of the uterus; in dysmenorrhea; in sexual impotence; and in backward physical-mental conditions, when thyroid extracts has not given results.

—W. H.

(HYPOPHYSIS) A peculiar form of pituitary disturbance. Appelbaum (E.), N. York M. J. [etc.], 1922, 115, 419.

Description of a case of Reichman's type of pituitary disorder. A woman of 21 years suffered with severe headaches for 10 years. weakness, anorexia of 3 years' duration, cyanosis of the face for 18 months, menstrual disturbances, exophthalmos and dilated pupils. She had acromegalic features, hands and feet; her heart was slightly hypertrophied to the left; the reflexes were normal. Urine was negative and Wassermann examination was negative. The red cell count was 4,550,000, the white 12,000. The differential count showed neutrophiles, 46 per cent; lymphocytes, 46 per cent; and transitional cells, 8 per cent. The spinal fluid showed 30 cells, a normal pressure, and was clear with a trace of globulin and it reduced Fehling's solution. X-ray examination showed erosions of the posterior clinoid process of the sella turcica.—H. W.

(HYPOPHYSIS) Three cases of supra-pituitary tumour presenting Fröhlich's syndrome. Armstrong (C. N.), *Brain* (Lond.), 1922, 45, 113-125.

Results of pre- and post-mortem examination of three cases are given. A male of 10, somewhat adipose, of feminine type, with normal genitalia, and reduced visual acuity, and a female, 35, enormously fat, with fine, soft, dry skin, small visual acuity, and some polyuria showed cystic ependymomas, walnut sized, flattening the pituitary, which appeared to be of normal size in the first. The third case, a female of 18 years, with the appearance of 12 to 14 years, childish, cheerful, very fat, with little body-hair and much diminished visual acuity, showed a cholesterol-containing cyst filling the sella turcica.—A. T. C.

(HYPOPHYSIS) Tumor of the PITUITARY, report of case. Baldauf (L. K.), *Kentucky M. J.* (Bowling Green), 1922, 20, 610-612.

The diagnosis of pituitary tumor was made on a man of 50 years because of drowsiness, rapid increase in weight, right temporal hemianopsia, nervousness and irritability, and sexual impotence. The Wassermann reaction was negative.—H. W.

(HYPOPHYSIS) The antidiuretic effect of pituitary extract applied intranasally in a case of DIABETES INSIPIDUS. Blumgart (H. L.), *Arch. Int. Med.* (Chicago), 1922, 29, 508-514.

The prompt though transitory effect of injections of pituitary extract in controlling the thirst and polyuria in diabetes insipidus is well known. If the extract is administered by mouth (even in gum drops), by colonic irrigation or by suppositories, this beneficial action is not obtained. Injections, however, are inconvenient and expensive and difficult for long continued use. A patient was studied whose daily urine output was 6 to 9 liters. Injection of only 0.005 cc. of pituitrin "O" (Parke Davis) was promptly effective in markedly diminishing urinary output. Pituitrin by mouth, posterior pituitary tablets by mouth, pituitary extract by rectum, lumbar puncture, and histamin sprayed, swallowed or subcutaneously were entirely ineffectual. Extract of the posterior lobe (1.5 cc.) sprayed intranasally every three or four hours controlled and checked the polydypsia and polyuria just as effectively as when administered by injection. The author believes that the effect of pituitary extract intranasally and subcutaneously is a diminution of the water intake and urinary output with a corresponding alleviation of thirst, a rise in the specific gravity of the urine and a dilution of the blood.—H. L.

HYPOPHYSIS and its posterior lobe considered pharmacologically. Borrien (V.), *J. de pharm. et chim.* (Par.), 1922, 25, 344-348.

The active principle of the posterior lobe is very diffusive in H₂O and EtOH, is analogous in comparison to adrenaline, but thus

far has not been isolated. To preserve the lobes for several days after collection, weigh, then immerse them in a small amount of physiological 0.7% solution to which 0.5% PhOH and 5 to 6 drops of AcOH per 100 cc. are added, and keep the preparation in a well corked flask.—Chem. Abst., 16, 2574.

(HYPOPHYSIS) DIABETES INSIPIDUS. Cables (H. A.), Illinois M. J. (Oak Park), 1921, 40, 28.

A brief review of etiological theories and diagnosis of diabetes insipidus, with report of three cases in married women. In the first patient, 35 years of age, the polyuria dates from the age of 12, with a quantity of 8½ quarts daily, and a specific gravity of 1001. The second, 25 years old, dates her condition from the age of 13, following an attack of measles. In this case the quantity was 8 quarts; the specific gravity, 1002. The third patient, 33 years old, suffered with polyuria from the time of an attack of scarlatina 12 years before. The quantity was 7 quarts; the specific gravity, 1002. In each of these cases the administration of desiccated whole pituitary gland resulted in immediate relief, which thus far appears permanent. With a decrease of urinary output there was an increase of urinary concentration to normal.—I. B.

A case of DIABETES INSIPIDUS due to lesion of the infundibulum (Un cas de diabète insipide par lésion de l'infundibulum). Camus (J.), Roussy (G.) & Le Grand (A.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 719-722.

The patient was admitted to the hospital for epileptiform convulsions and fugitive paralysis. There was an abundant polyuria (7-8 liters) without glycosuria. Injection of extracts of the posterior lobe of the pituitary resulted in lessening the polyuria by one liter; another time from 8 liters to 5½ liters; a third time it had no effect. It could also be reduced by antipyrine, novocaine, and lumbar puncture. Death occurred after an attack of severe vomiting. At autopsy there was found an abscess the size of a small nut which destroyed the pituitary entirely. Macroscopically, there was no apparent lesion of the infundibulum. Microscopically, however, there were important interstitial and cellular lesions of the opto-peduncular region comparable in all points to those described by Lhermitte. The authors point out that a simple macroscopic examination of this case would confirm the hypophyseal origin of polyuria, but the microscopical examination shows the polyuria to have been due to a lesion of the nuclei of the infundibulum and tuber cinereum.

—T. C. B.

HYPOPHYSECTOMY in the dog and the cat. Technique and results of 149 operations (Hypophysectomie chez le chien et le chat. Technique et resultats de 149 interventions). Camus (J.) & Roussy (G.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1008-1010.

Numerous observations on the physiology of the hypophysis have not definitely established whether it is essential to life. The authors have operated on 122 dogs and 27 cats, using both the buccal and the temporal route in removing the hypophysis. Of 98 dogs operated upon through the mouth, 22 died during the operation, or in less than 24 hours after; 35 died in a few days; 14 in a few weeks; 12 in from 2 to 11 months; 12 were sacrificed a long time after the operation; the rest were living at the time of writing. Of those operated upon by the temporal route, 7 died in less than 24 hours; 8 in a few days; 2 in a few weeks. The rest are still living. Similar results were obtained in cats. In the majority of cases where death followed total ablation of the hypophysis the autopsy showed either meningitis, hemorrhage or lesion extending to the base of the brain. The possible causes of death are discussed and it is concluded that the hypophysis is not necessary to life.—T. C. B.

(HYPOPHYSIS) *Anatomo-pathological study of experimental lesions causing polyuria and the adiposogenital syndrome in the dog (Etude anatomo-pathologique des lésions polyurique et le syndrome adipo-génital chez le chien).* Camus (J.), Roussy (G.) & Le Grand (A.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1070-1073.

A description of the lesions found in some of the most pronounced cases of polyuria and adiposogenitalis occurring in a series of 149 dogs, previously reported, in which an experimental lesion in the opto-peduncular region had been made.—T. C. B.

(HYPOPHYSIS) *Case of hypopituitary disorder (Fall von Hypopituitarismus).* Cieszynski (F. K.), *Przegl. lek. (Kraków)*, 1921, 60, No. 4.

A boy of 13 years of underdeveloped height, with typically developed fat deposits, testicle agenesis and a somewhat myxedematous skin. Since no significant tumor of the hypophysis was in evidence the author considers it a case of hypofunction.—F. S. H.

(HYPOPHYSIS) *Study of some cases of DIABETES INSIPIDUS with special reference to the detection of changes in the blood when water is taken or withheld.* Christie (C. D.) & Stewart (G. N.), *Arch. Int. Med. (Chicago)*, 1922, 29, 555-566.

The regulation of the excretion of water by the kidneys was studied in two cases of diabetes insipidus presenting the typical features, and in one case of polyuria of acute onset, apparently associated with a brain lesion. In the last case the polyuria (12 liters per day) disappeared permanently after lumbar puncture. Blood specimens obtained immediately before and immediately after a long period of complete deprivation of water (24 hours or more) showed no definite differences in the electrical conductivity of the

serum, which could be associated with changes in the rate at which water was being absorbed, transported and excreted, although the conductivity can be measured with great accuracy. The same was true of the percentage volume of serum. The various tests of efficiency of renal function gave normal result. When pituitary extract was administered the kidney showed normal powers of concentrating the urine.—H. L.

Influence of the HYPOPHYSIS on dysfunction of the sexual organs (*Der Einfluss der Hypophyse auf die Dysfunktion der Genitalorganen*). Dietrich, *Klin. Wchnschr. (Berl.)*, 1922, 1, 1760.

A short note. The author describes a case of "adipositas hypogenitalis hypophysaria" which is a "forme fruste" of Fröhlich's disease. After injection of adrenalin hyperglycemia is retarded. No details are given.—J. K.

(HYPOPHYSIS) The normal sella. Enfield (C. D.), *J. Am. M. Ass. (Chicago)*, 1922, 79, 934-935.

Roentgenograms of 100 cases of all types of disease, excluding endocrine disturbance and "pituitary types," were taken with a view to establishing a normal if such could be done. With the technique used Enfield finds the width varying from 6 to 19 millimeters and the depth from 3 to 12 millimeters. Outline tracings from 9 cases are given. He finds a female preponderance in the so-called closed type and a male preponderance in the unusually large ones. The size of the sella was not proportionate to the size of the body. His general conclusion is that the only definitely abnormal roentgenographic finding is clear evidence of erosion of the bony structure.—W. M. A.

(HYPOPHYSIS) Glycosurie dans l'ACROMEGALIE. Etienne (G.), Drouet (L.) & Yovanovitch-Brintcheva (B.), *Rev. méd. de l'est (Paris & Nancy)*, 1922, 50, 271-279.

A woman of 37 years is described. The sella turcica was enlarged. She gave a positive Goetsch test. Severe glucosuria was present. There was an enlarged thymus. The diagnosis of glucosuria of hypophyseal origin is given. Hyperactivity of adrenal function is also admitted as a possibility.—F. S. H.

(HYPOPHYSIS) A case of acromegalic gigantism (*Sobre un caso de gigantismo acromegálico*). Flóres (N.) & Dias (A.), *Rev. dos Cursos de la Fac. de med. (Porto Alegre, Brazil)*, 1921, 7, 159-174.

This article can not be too highly praised for its completeness in description and the manner of presentation. It is well illustrated with splendid photographs and reproductions of the x-ray pictures. The case described is one of typical acromegalic gigantism.—F. S. H.

HYPOPHYSEAL syndromes of gestation. Acromegaly of pregnancy (Syndromes hypophysaires et gestation. Acromégalie gravidique). Fruhinsholz (A.), Rev. méd. de l'est (Paris & Nancy), 1922, 50, 255-264.

A case report of a woman who, during pregnancy, developed the syndrome of a mild but typical acromegalic condition which receded after delivery and nursing.—F. S. H.

The rôle of the HYPOPHYSIS and of the brain in the production of cutaneous alterations in the toad (Le rôle de l'hypophyse et du cerveau dans la production des altérations cutanées chez le crapaud). Giusti (H.) & Houssay (B. A.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1112-1113.

Extirpation of the hypophysis in the toad, *Bufo marinus* (L.), produces an intense and curious alteration of the skin. The operations, which were through the mouth, caused in all cases a bronzing or blackening of the skin commencing 4 to 5 days after operation (in the spring), later in winter (8 to 15 days). Daily ingestion or injection of hypophyseal extract did not prevent it. In the spring there was an expulsion of eggs from the females, which was thought to be due to injury of the perihypophyseal zone.—T. C. B.

(HYPOPHYSIS) Acromegaly and lymphatic leukemia. Goldstein (H. I.), Am. Physician (Rahway, N. J.), 1922, 27, 286-288.

A case of acromegaly with lymphatic leukemia that has been under observation for over ten years, is reported by the author. The unusual features of the case are the absence of pressure symptoms or "neighborhood symptoms," the loss of sexual power, for a period of six years or more, followed recently, for the past two and a half years, by a return of all sexual power, desire, and function; the occurrence of lymphatic leukemia, with splenomegaly and lymphomegaly for the past sixteen months. Improvement followed Roentgen-ray treatment to the spleen, lymph glands, pituitary and long bones. No other case of acromegaly has been found recorded in the literature, associated with leukemia, and such large sella turcica and without ocular disturbances, or any pathological changes in the eye-grounds, and with a normal basal metabolic rate.

—Quoted from original.

(HYPOPHYSIS) The oral administration of pituitary extract. Hamill (P.), Proc. Roy. Soc. Med. (Lond.), 1921, 14, 17-19.

Though thyroid extract administered by mouth is known to produce definite results, such is not the case with most other incretory gland products. In a series of experiments carried out on cats, Hamill found that solutions of pituitary extract administered by mouth resulted in characteristic reactions. It was observed that absorption takes place from the stomach and is more rapid when

the organ is full and actively digesting. Moderate doses produce the usual uterine contractions; large doses give rise to colicky contractions of the intestines, and vomiting. The author concludes that pituitary extract orally administered to human beings is of definite clinical use and should be administered in solution on a full stomach.—I. B.

HYPOPHYSIS and carbohydrate metabolism (*Hypophyse et métabolisme hydrocarbone*). Houssay (B. A.), Hug (E.) & Malamud (T.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1115-1116.

All experiments were on dogs. After a lengthy study of the relation of the hypophysis to carbohydrate metabolism, the following conclusions are given. There is often glycosuria, not intense during the first days following extirpation of the hypophysis, piqûre, or a lesion of the neighboring cerebral zone. Dogs with the hypophysis extirpated, or with a lesion of the neighboring zone generally have a normal tolerance for the injection of sugar; but some dogs with marked adiposo-genital dystrophy tolerate large doses of sugar. In testing the tolerance by slow intravenous injection hyperglycemia curves are similar in hypophysectomized and control animals. Glycemia and the percentage of glycogen in the muscles and liver are normal in hypophysectomized animals.—T. C. B.

(HYPOPHYSIS) Normal and abnormal variations of the PITUITARY fossa. Howe (H. S.), *Neurol. Bull. Columbia University*, 1919, 2, 233-238.

Howe has measured and made tracings of the pituitary fossae of forty normal skulls and has found that this fossa is normally subject to great variations both in size and outline. Radiograms, therefore, give no information of the condition of the pituitary gland unless the sellar enlargement, or the amount of absorption of the bone is very great. He figures normal fossae showing all degrees of openness, of depth, and of width. He points out that although the anterior clinoid processes, as seen on an x-ray plate, seem to form the anterior portion of the sella, this is an artefact of projection; the true anterior superior boundary is the tuberculum sellae. In acromegaly there may be (1) no change in the size or outline of the sella; (2) general enlargement of the sellar space without erosion or absorption of bone; or (3) enlargement with absorption of all or part of the bony envelope. The normal hypophysis about fills the pituitary fossa transversely but not anteroposteriorly, so that there is room for some enlargement, by pressure on the circular Curis sinus, before the bony cavity is filled. It is frequently in acromegaly that the fossa has been enlarged by the absorption of bone. The floor of the sella or its anterior or posterior wall with splendid before the tips of the posterior clinoid processes or the dorsum sellae. Supra-tentorial tumors and conditions The case desc.

causing chronic increase of intracranial pressure may induce absorption of the posterior clinoid processes.—Med. Sc., 6, 488-489.

An experimental study of the PANCREAS and HYPOPHYSIS inter-relationship (Pankreas und Hypophyse. Eine tierversperimentelle Studie). Kraus (E. J.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1921, 68, 258-277.

In an earlier paper (Virchow's Arch. f. path. Anat. [etc.], 1920, 228, 68), the author described the anatomical changes in the human hypophysis in cases of diabetes mellitus. These changes were characterized by a noteworthy reduction in the size of the anterior lobe of the pituitary with great reduction in the number of acidophilic cells. The present communication deals with his efforts to reproduce these hypophyseal changes in cats by complete and partial removal of the pancreas. Eighteen partially or completely depancreatized cats and ten controls were studied. He found a distinct decrease in the size of the anterior lobe and in the number of acidophilic cells in the depancreatized animals. Atrophic changes were also noted in the intermediate and posterior lobes. He also observed morphological evidence of increased thyroid activity following pancreatectomy. This is an acute reaction, and if the animals survive some weeks definite atrophic changes supervene. He noted also a definite decrease in the lipid material of the suprarenal cortex and the chromaffin reaction of the medulla. In the testes atrophy of the tubules with cessation of spermatogenesis and regressive changes in the nuclei of the interstitial cells was observed. There were atrophic changes in the pineal gland, while the parathyroids showed no definite changes.—D. M.

The influence of the HYPOPHYSIS upon the tonicity of the capillaries (Sur l'influence de l'hypophyse sur la tonicité des capillaires). Krogh (A.) & Rehberg (P. B.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 461-463.

Krogh and Harrop have demonstrated in the blood of mammals a substance which is capable of maintaining the tonicity of the capillaries in the interdigital membrane of the frog. It can be extracted by dialysis, resists boiling for a short time, is insoluble in alcohol, and is precipitated by phosphotungstic acid. It is said that extirpation of the hypophysis may produce subcutaneous edema. The authors find that removal of the hypophysis or of the "lobe intermédiaire" induces characteristic alterations in the capillary activity of the skin. The capillaries relax, while the arteries undergo no alteration. This lasts for days or weeks and is followed by a failure of vasomotor equilibrium. There is extreme contraction of arteries and capillaries, alternating at intervals with normal dilatation of the arteries and extreme dilatation of the capillaries. By perfusion of the hind legs with a suspension of washed beef corpuscles

in Ringer-gum solution isotonic with frog's blood, the circulation is rendered visible. The perfusion is made rhythmic by a special apparatus to be described later, and the normal systolic pressure is maintained. The perfusion of Ringer-gum solution is soon followed by such an alteration in the permeability of the capillaries that there is extravasation even of the colloids. If pituitrin (P. D. & Co.), is added, 1:10,000, the contraction of the capillaries and arteries is so marked that the circulation is reduced to a minimum, or completely arrested. Pituitrin 1:50,000 and up to 1:500,000 is without effect on the arteries, but maintains the normal contractility of the capillaries. These reactions are analogous to those of the constrictor substance obtained from mammalian blood; pituitrin is dialysable, is precipitated by phosphotungstic acid, resists heat, and is insoluble in alcohol; and the conclusion is drawn that the hypophysis constantly secretes a substance which circulates in a low concentration and maintains the tonicity of the capillaries.—T. C. B.

(HYPOPHYSIS) Pituitary disorders in their relation to acromegaly (hyper-pituitarism), with suggestions for the use of a more precise terminology. Krumbhaar (E. B.), Arch. Diagn. (N. Y.), 1922, 14, 213-239.

. An illustrated histo-pathological study of acromegaly. The results lead to the theory that acromegaly is due to (or at least follows) hyperfunction of the anterior lobe, after ossification of the epiphyses, as expressed by an increase in acidophile cells. The acidophile increase may be expressed either as a hyperplasia of the normal lobe or as an adenoma. After the development of acromegaly the pituitary lesion may undergo cystic degeneration, so that lesions of this nature do not necessarily contradict the theory. Pituitary tumors may exist for many months even to the extent of destroying both lobes, without giving obvious signs of so-called pituitary disease. It is probable, however, that in most, or all, of these cases careful functional tests would reveal a latent disorder. The author recommends the following terminology which is self-explanatory: hyper-pre-pituitarism, hypo-pre-pituitarism, hyper-post-pituitarism, hypo-post-pituitarism and dispituitarism.—F. S. H.

(HYPOPHYSIS) ACROMEGALY and infantile gigantism in childhood (Ein Beitrag zur Akromegalie und zum infantilen Riesenswuchs im Kindesalter). Kundratitz (K.), Jahrb. f. Kinderh. (Berlin), 1922, 98, 292-298.

A review of the literature dealing with the different roles of the hypophysis and the gonads in the development of cases of acromegaly and infantile gigantism. Both conditions may be present either alone or in combination. The author describes a boy of 10, 142 cm. in height and weighing 39 kg. that showed characteristics of both conditions.—C. H. G.

(DIABETES) Renal glycosuria. Lewis (D. S.), Arch. Int. Med. (Chicago), 1922, 29, 418-427.

The four cardinal points in diagnosis are (a) glycosuria without hyperglycemia; (b) little, if any relationship between the carbohydrate intake and the amount of glucose excreted in the urine; (c) the absence of the signs and symptoms of diabetes mellitus, and (d) a long period of observation during which the patient shows no tendency to develop diabetes mellitus. In this paper one case is reported which fulfills all of the four requirements (having been observed for six years), and two cases are reported which answer the first three tests (having been observed for twelve months and fifteen months, respectively). The first case is of unknown origin; the blood sugar curve is of a strictly normal order. The second and third cases belong in the other group associated with chronic diffuse nephritis or arteriosclerosis, in which the patient shows a remarkably high and prolonged rise in the blood sugar, which is probably a retention phenomenon or perhaps connected with the high diastatic activity of the blood so often seen in severe nephritis.—H. L.

HYPOPHYSEAL origin and treatment of two cases of idiopathic **DIABETES INSIPIDUS** of familiar form (Sobre dos casos de diabetes insipida idiopatica de forma familiar y su tratamiento por el principio hipofisario). Martinez (G. N.) & Navarro (A.), Rev. del Circulo med. de Cordoba, 1922, 10, 78.

Two cases of diabetes insipidus are reported in father and son in a family in which there were other cases. The author believes that one cannot dispute the hypophyseal origin of this disease.

—B. A. H.

Polyurie HYPOPHYSIAIRE. Minet (J.) & Auguste, Réunion méd.-chir. des hop. de Lille, 1922, July 27; abst., Presse méd. (Par.), 1922, 30, 684.

The authors observed a man in poor general health and with diabetes insipidus, in whom only one injection of 0.10 gm. of hypophyseal extract was sufficient definitely to bring the urine output to normal. The authors believe that the trouble was due to a relatively slight disturbance of the hypophyseal function caused by general nutritional disorders.—R. G. H.

HYPOPHYSEAL dwarfism. Marañón (G.) & Solanilla (L.), Arch. españ. de pediat. (Madrid), 1921, 5, 467, abst., Monatschr. f. Kinderh. (Leipz.), 1922, 23, 231.

Description of a characteristic case of dystrophia adiposogenitalis with dwarfism. Roentgenographically there was shown defective development of the metacarpals and a small sella turcica. Organotherapy was tried without result. The condition was referred to a sclerosis of the anterior lobe of the pituitary which was related to tuberculosis in the mother.—C. H. G.

(HYPOPHYSIS) PITUITARY gland therapy. Ohler (W. R.) Boston M. & S. J., 1922, 187, 173-174.

This is a short statement of the manifestations of dispituitarism, followed by a plea for more careful observation of the results of treatment with pituitary substance. There are no new data.

—J. C. D.

(HYPOPHYSIS) A case of acromegaly and gigantism with mental troubles (Un cas d'acromegalogigantisme avec troubles mentaux). Parhon (C.) & Stocker (A.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1920, 2, 2-4.

The mental disturbance accompanying the acromegaly was emotional neurasthenia.—F. S. H.

The functional value of the HYPOPHYSIS and the clinical means of evaluation (La valeur fonctionnelle de l'hypophyse et les moyens cliniques de l'évaluer). Parisot (J.) & Richard (G.), Rev. méd. de l'est (Paris & Nancy), 1922, 50, 279-285.

A review with no new data.—F. S. H.

Action of HYPOPHYSIN (Parke Davis's pituitrin) on the rabbit's pupil. Pollock (W. B. I.), Brit. J. Ophth. (Lond.), 1920, 4, 106-124.

Instilled into the eye, midriasis occurred in 94% of cases; this effect is increased by "decentralization," and still more by "deanglionation," of either the sphincter pupillæ or the dilator iridis, or better still of both. Given intravenously, the local effect may be overlooked if counteracted by a rise of blood-pressure or excitation of the 3rd nerve. If that nerve is cut, dilatation of the pupil by pituitrin (intravenously) is marked and immediate. It is considered that the drug, like adrenaline, acts on the myoneural junction.

—Physiol. Abst., 5, 248.

Radium and x-ray in tumors of the HYPOPHYSIS. Quick (D.), Arch. Ophth. (N. Y.), 1920, 49, 256.

The author points out that examination with the ophthalmoscope and x-rays is usually conclusive and that the latter is particularly useful when bony destruction is noted. The pathology of tumours of the hypophysis is shortly dealt with. A review of surgery on these types of cases and of the results follows, from which the author concludes that it is far from being the ideal form of treatment. The results of treatment by many radiologists are given; in every case there was some improvement in the symptoms by using radium and x-ray either together or separately. The author then describes three cases that came under his personal notice and the procedure of treatment. Radium alone was used, and the author thinks that possibly this was a mistake. He points out that if the

patient be suffering from coryza or any nasal infection there is danger of death from meningitis. Three points are put forward in favor of radiological treatment: (1) there is no operative mortality; (2) pressure symptoms respond much more promptly and more uniformly and without pain or inconvenience; (3) it offers hope of benefit to every type of case except perhaps simple cysts, whereas the scope of surgery is limited. Other reasons for employing radiotherapy are also dealt with, and the advantages and disadvantages of x-rays and radium are discussed. On the whole the author favors the application of radium after a submucous resection of the septum nasi and possibly the removal of a window from the floor of the sella turcica so as to expose the gland directly.—*Med. Sc.* 6, 433-434.

A method for the study of the human HYPOPHYSIS cerebri, with illustrative results. Rasmussen (A. T.) & Herrick (Ruth), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1922, 19, 416-423.

Report of the determination of the relative and absolute weights of the three principle parts of the main body of the hypophysis, together with the relative number and arrangement of the three types of cells in pars anterior of normal adult males between 20 and 60 years of age. The large colloid masses were included in the study. Post-mortem material was used and fixed in ordinary formalin. The results are given in a table, the details of which cannot be abstracted.—*F. S. H.*

(HYPOPHYSIS) Traumatic lesions of the pituitary body. Reverchon (L.) & Worms (G.), *Bull. et mém. Soc. de chir. de Par.*, 1921.

The authors give details of a case of fractured base of the skull. The patient was under observation for several months with bilateral paralysis of the fifth, sixth and seventh cranial nerves and with signs of a pituitary lesion. Autopsy revealed a pituitary gland which was reduced to a mere nodule and was surrounded by a dense capsule of fibrous tissue. The pituitary symptoms were polydipsia, polyuria, marked anemia and asthenia, arterial hypotension and a psychical state of puerility and apathy. Lesions of the pituitary gland should henceforth find a place in the complications of basal fracture.

—*Med. J. Australia*, 1921, ii, 86.

Danger of HYPOPHYSIS extracts (A propos du danger des extraits d' hypophyse). Riehl, *Bull. Soc. d'obst. et de gynéc. de Par.*, 1922, 11, 396-403.

Supports the belief of Doederlein that pituitary extracts should be used in labor with caution and only towards the end of the period of dilatation or period of expulsion, and only when parturition is sufficiently advanced to make possible instrumental interference if necessary.—*F. S. H.*

(HYPOPHYSIS) Discussion of the report of Le Lorier on the subject of the use of sublimate and PITUITARY extracts by midwives

(Discussion du rapport de M. Le Lorier: au sujet de l'emploi du sublimé et des extraits hypophysaires par les sages-femmes). Rouvier, Pouget & Laffont, Bull. Soc. d'obst. et de gynéc. de Par., 1922, 11, 162-163.

The prevention of the use of pituitary extracts by midwives was recommended.—F. S. H.

(HYPOPHYSIS) Rupture of uterus at term following an injection of PITUITARY extract (Rupture d'un utérus à terme à la suite d'une injection d'extrait hypophysaire). Séjournet & Braine, Gynécologie (Par.), 1922, 21, 271-283; Bull. d'obst. et. gynéc. de Par., 1922, 11, 234-237.

A case description with no conclusion. The patient recovered.
—F. S. H.

Action of extracts of the HYPOPHYSIS, the THYROID and the SPLEEN, injected into the lateral ventricles of the brain (Action produite par les extraits d'hypophyse, de thyroïde et de rate injectés dans les ventricules latéraux du cerveau). Stern (L.), Battelli (F.) & Jauffret (J.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 753-754.

Fresh aqueous extracts of the glands were injected into the lateral ventricle of the dog and the guinea pig. In general the results were analogous in the two species. The amount injected varied with the size of the animal. Extract of the posterior lobe of the beef pituitary generally had no immediate effect. Occasionally there was a slight phase of excitation in the guinea pig. After a time there developed a state of somnolence which augmented little by little, lasted several hours and then the animal gradually recovered its normal condition. In the guinea pig there was diminution of body temperature, but there was no appreciable change in the dog. There was slight glycosuria in the guinea pig. Extracts of the anterior lobe of the hypophysis produced no appreciable effect. Extract of spleen immediately produced a state of excitation with violent muscular contractions, subsultus, etc. This condition was rapidly succeeded by a state of prostration with muscular feebleness, and slight paralysis. There were no significant changes in temperature. In the dog there was an abundant secretion of watery saliva. The effects of extract of muscle were analogous to those of the spleen. Extract of thyroid was inconsistent in effects. Sometimes there was violent agitation, sometimes no effect; in some elevation of temperature, in others slight diminution was seen.

—T. C. B.

The HYPOPHYSIS in mental diseases (L'hypophyse dans les maladies mentales). Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 124-131.

Series of cursory observations.—F. S. H.

HYPOPHYSEAL cyanophilia in epilepsy (*La cyanophilie hypophysaire dans l'épilepsie*). Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 70-77.

Histological studies of the hypophyses of individuals who have had epilepsy showed a marked constancy in the occurrence of a multiplication of the cyanophile elements of the epithelial lobe.

—F. S. H.

(HYPOPHYSIS) The so-called permanent polyuria of experimental DIABETES INSIPIDUS. Towne (E. B.), Proc. Soc. Exptl. Biol. & Med., 1922, 21, 1-4.
 exostosis of the bone or a very slow growing tumor with much calcareous deposit. Radioscopy in the second showed a normal sella turcica. Treatment with anterior lobe of pituitary led to no improvement in any of these cases.—A. T. C.

(HYPOPHYSIS) Studies in DIABETES INSIPIDUS, water balance and water intoxication. Weir (J. F.), Larson (E. E.) & Rown-tree (L. G.), Arch. Int. Med. (Chicago), 1922, 29, 306-330.

Fifteen cases of diabetes insipidus were studied. One patient had a supratentorial brain tumor, another a hypophyseal tumor, four had syphilis; in nine cases no causative factor could be determined. Antisyphilitic treatment had no significant effect on the diabetes insipidus in the four syphilitics. The symptom of thirst is not due to dryness of the oral mucous membranes, because cocainization of the mouth and nasopharynx had no effect on the polydipsia and polyuria. Careful studies of renal function failed to incriminate any part of the urinary tract as an etiologic factor and revealed no deviations from normal function. All fifteen cases responded promptly and beneficially to injections of posterior lobe pituitary; tends to inhibit hypersomnia and has a favorable effect on the asthenia of Parkinson's disease.—F. S. H.

(HYPOPHYSIS) Diffuse painful adiposity accompanied by changes in the sella turcica (*Adipose douloureuse avec modifications de la sella turcique*). Vallery-Radot (P.) & Dollfus (M. A.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1016-1022.

A case report with no unusual data.—F. S. H.

Exaggeration of carbohydrate tolerance, and absence of reaction to extract of posterior lobe of the HYPOPHYSIS in a case of ACROMEGALY (*Exagération de la tolérance aux hydrates de carbone et absence de réaction à l'extrait de lobe postérieur de l'hypophyse chez une acromégالية*). Verger (H.), Massias (C.) & Auriat (G.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 197-198.

The subject was a woman of 36 with epileptic crises for 13 years with hirsutism, and a modified acromegaly limited to the face, the hands and feet remaining normal. Radiography showed

very drowsy, and later showed muscular twitching and ataxia, and finally convulsions and coma.—H. L.

HYPOPHYSEAL nanism (*Hypophysärer Zwergwuchs*). Witthauer, *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1025.

Demonstration of a dwarf of 24 with dystrophia adiposogenitalis. The sella was very large. No other details are given.
—J. K.

The PARATHYROID. Bergstrand (H.), *Nord. med. Ark. (Stockholm)*, 1920, 53, 791-856.

Mainly anatomical. The Bielchowsky method of staining is recommended for parathyroid tissue. Only one cellular type of functional value was found. Welch's cell is a degeneration product. Colloid material was found which is either a true secretion or a product of the breakdown of the Welch cell.—R. G. H.

A case of TETANY in a growing boy, together with some critical remarks on the pathogenesis of tetany (*Ein Fall von Tetanie bei einem Erwachsenen nebst einigen kritischen Bemerkungen hinsichtlich der Pathogenese der Tetanie*). Bolten (G. C.), *Monatschr. f. Psychiat. u. Neurol. (Berl.)*, 1917, 42, 211-236.

A description of a classical case of tetany. The tetany was probably of parathyroid origin largely since dentition was faulty and cataract was present. A general pluriglandular disturbance was also suspected. The Wassermann reaction was positive. After reviewing the literature of similar cases and discussing them, Bolten concludes that all cases of tetany cannot be considered as of parathyroid origin or that the tetany poison is always the same.—F. S. H.

Epilepsie und TETANIE. Bolten (G. C.), *Deutsche Ztschr. f. Nervenhe. (Leipz.)*, 1917, 57, 160-202.

Epilepsy is classified under four headings: (a) cerebral epilepsy, (b) epilepsy due to endogenous intoxications (c) epilepsy due to exogenous intoxications, and (d) genuine epilepsy due to thyroid and parathyroid insufficiency. In the last group there is placed infantile tetany, spasmophilia, post-operative tetany after strumectomy and induced tetany in animals. A good review of the subject given in the title accompanied by many references.—F. S. H.

Reticular apparatus of Golgi and secretory polarity of the PARATHYROID cells (*Appareil réticulé de Golgi et polarité sécrétoire des cellules parathyroïdiennes*). Courrier (R.) & Reiss (P.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 867-868.

Histological.—T. C. B.

A case with symptoms of paralysis agitans with excessive calcium output in the urine—improvement under PARATHYROID treat-

ment. Dercum (F. X.), J. Nerv. & Ment. Dis. (N. Y.), 1918, 47, 368.

The author reports a case of a married woman of 57 who presented symptoms suggesting early paralysis agitans. The symptoms had been present a year and included fixed facial expression and a tendency to hold fixed positions of the hands and body. Laboratory findings were negative except for an excessive output of calcium in the urine—0.532 gms. Under the administration of parathyroid extract, 1/20 grain three times daily, the symptoms improved markedly and within a month had completely disappeared. The calcium output in the urine continued over 0.5 gm. No blood calcium determinations were given. The improvement was attributed to the administration of the parathyroid extract, which did not seem to have any influence on the calcium output. Dr. Burr reported a series of about 13 cases of paralysis agitans treated with parathyroid with improvement in one case and no change in the remaining 12.

—F. H. A.

(PARATHYROID) TETANY, a report of cases with acid-base disturbance. Grant (S. B.), Arch. Int. Med. (Chicago), 1922, 30, 355-361.

The occurrence of tetany in various disorders of the body is discussed. These disorders may be divided into two groups: (a) pyloric obstruction, hyperpnea and overdosage with sodium bicarbonate, which have in common a disturbance of the acid-base equilibrium, due to an increase in the ratio of sodium bicarbonate to carbonic acid in the blood; and (b) infantile tetany and parathyroid tetany, in which there is a calcium deficiency in the blood. Six cases of tetany in adults, all of the type in which there was an acid-base disturbance, are reported. Three cases occurred in obstruction of the stomach. In two of these the plasma carbon dioxide capacity was found greatly increased. In one, the blood chlorid was found markedly decreased. Serum calcium in this case was in the upper limits of normal. These results corroborate in man the experimental findings of investigators in animals. Two cases resulted from overdosage with sodium bicarbonate, and one occurred in hysterical hyperpnea.—H. L.

(PARATHYROID) The supposed relation between alkalosis and TETANY. Greenwald (I.), J. Biol. Chem. (Balt.), 1922, 54, 285-304.

After a general discussion of the various theories of tetany, Greenwald presents the results and interpretations of his experiments with dogs, in which tetany was induced by the administration of sodium carbonate or bicarbonate. Analyses of the blood showed that after such injections there is a retention of carbon dioxide which is so great that the reaction is changed only slightly. When

convulsions appear the bicarbonate content of the blood and the alkalinity begin to diminish and this process continues so that before death both may be less than normal. The change is due in part to the increased production of lactic acid. The production of lactic acid appears to be increased before convulsions appear, but is enormously accelerated thereby. The concentration of sodium in the plasma at the time the convulsions appear is the same as that found when other sodium salts are administered, and hence the tetany is ascribed to a "sodium poisoning," a disturbance due to an excess of sodium, of the normal equilibrium between sodium and other ions. Parathyroid tetany is not an alkalosis.—F. S. H.

The metabolism of inorganic salts. I. The organic ion balance of the blood in PARATHYROID tetany. Gross (E. G.) & Underhill (F. P.), *J. Biol. Chem. (Balt.)*, 1922, 54, 105-120.

A series of decisive experiments were performed on dogs showing that the blood salts in these animals under normal fasting conditions are practically constant, that parathyroidectomy chiefly disturbs the ratio between calcium and potassium, and that the inception of tetany obtains with a definite change in the ratio of calcium to potassium. The hypothesis is suggested that both low calcium and high potassium are factors in the production of the increased irritability. (The suggestion that the disturbances in salt relationships in the blood are factors in the production of the increased irritability was made some time ago by the abstracter.)—F. S. H.

The probable function of the PARATHYROID glands. Hammett (F. S.), *N. York M. J. [etc.]*, 1922, 115, 401-403.

The metabolism of muscle tone differs from that of muscle movement. Creatine, an important product of muscle tone, is relatively innocuous for the organism. Creatine is changed to creatinine by the loss of one molecule of water and is excreted in the urine. Creatine is acetylated methyl-guanidine. Methyl-guanidine is highly toxic and acts as an irritant to the nerve endings. Following parathyroidectomy methyl-guanidine accumulates from the existent condition of muscle tone. Hence, it is probable that the function of the parathyroid glands is the elaboration of a secretion which assists in the prevention of the accumulation in the organism of the toxic nerve irritant, methyl-guanidine, which normally is a by-product of that phase of muscle metabolism concerned in muscle tone. This conclusion is borne out by the finding that animals of high muscle tone succumb more rapidly to parathyroidectomy than those with low muscle tone. According to the author there is not sufficient clinical nor experimental evidence to warrant the assumption that paralysis agitans, epilepsy, eclampsia, gastric tetany and convulsive states are resultant conditions of parathyroid deficiency.—H. W.

Report of a case of **PARATHYROID** insufficiency. Hurst (A. F.),
N. York M. J. [etc.], 1922, 115, 403-404.

A case reported of a male, age 47, a clerk who had a goiter at 30, was operated upon in 1908 and was well until August, 1910. He suddenly became depressed, nervous and restless, slept little, walked the greater part of the night, was tremulous and had fibrillary twitching of eye lids. There was no evidence of tetany, nor of goiter. The patient lost weight. He had difficulty in swallowing, felt irregular intestinal pains, had a pulse of 120, and palpitation. His face and neck were flushed; his hair ceased to grow, but did not become thinner. He became impotent. There were 3 to 4 large stools a day. The urine was scanty; the sweat was unaffected. The patient was put to bed in December. He gradually lost in spite of forced feeding and rest. Large doses of morphin and bromides were administered. Thyroid preparations aggravated the condition. He returned to work in February. On Jan. 18 he was placed on 1/10 grains of parathyroid four times a day. He slept better, was less restless, tremor and dysphagia improved, hair began to grow, the amount of urine increased, the stools diminished in bulk, the pulse fell below normal, libido returned, and he gained weight. He was perfectly well for five years (1918), at the end of which time there was slight recurrence of symptoms. He was again placed on parathyroid medication, and became perfectly well and remained so up to the time of this report.—H. W.

(**PARATHYROID**) The pharmacology of guanidin (Beiträge zur pharmakologischen Wirkung des Guanidins). Klinger (R.), Arch. f. exper. Path. u. Pharmakol. (Leipz.), 1921, 90, 129-141.

This is a study of the effects of guanidin and its methyl derivatives on cats and rats. In cats these substances cause an increase in the motor and psychic irritability beginning with unrest, twitching of the feet, and increasingly frequent convulsions of separate muscle groups up to strong general muscular spasms appearing at brief intervals. Salivation and maximal pupil dilatation appear, especially during seizures. The somewhat different symptoms are also described in the rat. There are two differences noted between the symptoms of guanidin intoxication and postoperative tetany. In the former there is a ready appetite for two or three days, the animal being kept from eating only by the convulsions. In the latter, on the other hand, one of the earliest and almost never failing symptoms is the loss of appetite and refusal of food. The second difference is the unlike efficacy of calcium salts. Amounts of these salts which cause an improvement in post-operative tetany are without effect in guanidin intoxication.—F. A. H.

PARATHYROID deficiency and its treatment. Lahey (F. H.), Boston M. & S. J., 1922, 187, 170-173.

It is pointed out that the only proved form of parathyroid deficiency is that following the removal of these glands. The author, as the result of his own experience and that of others, concludes that calcium lactate by mouth is the most satisfactory method of controlling tetany following interference with the parathyroids. The use of preparations of the parathyroids have not met with success.

—J. C. D.

Habitual vomiting and TETANY (Vomissements habituels et tétanie). Lemaire (H.) & Olivier, Nourrisson (Par.), 1922, 10, 302-312.

Not endocrine.—F. S. H.

The control and cure of PARATHYROID tetany in normal and pregnant animals. Luckhardt (A. B.) & Rosenbloom (P. J.), Science (N. Y.), 1922, n. s. 56, 48-49.

These authors have found it possible to keep completely parathyroidectomized dogs alive even when fed a diet chiefly of meat by means of the intravenous injection of Ringer's solution. After maintaining this treatment for about 40 days no further injections are necessary if a moderate amount of meat is given and the animals do not become constipated. Pregnant dogs can be kept alive by similar treatment, but with more difficulty. It seems clear that tetany is caused by an exogenous poison derived chiefly from the proteins of the food, especially meat. One can precipitate an almost fatal attack of tetany 33 days after parathyroidectomy in 2 hours by feeding one-half pound of meat, especially if the latter is not fresh. None of the adult animals have shown signs of myxedema after seven months. The young animals born of and raised by parathyroidectomized mothers were perfectly healthy.—F. A. H.

The recurrence of acute PARATHYROID tetany in completely parathyroidectomized animals during the oestrous cycle. Luckhardt (A. B.) & Blumenstock (J.), Science (N. Y.), 1922, n. s. 56, 257-258.

A report based upon two dogs from which all parathyroids had been removed several months previously. They had recovered from the early attacks of tetany and were in excellent health until the oestrous cycle. At this time severe tetany reappeared. It is suggested that the tetany which occurs in partially strumectomized women during menstruation is due to hypofunction or absence of parathyroids.—F. A. H.

Pathology of TETANY (Beiträge zur Klinik und Pathologie der Tetanie). Spiegel (E.) & Elias (H.), Wien. Arch. f. innere Med., 1921, 2, 447.

Of no immediate endocrine interest.—F. S. H.

The influence of the sodium ion in the production of TETANY. Tisdall (F. F.), J. Biol. Chem. (Balt.), 1922, 54, 34-41.

Not of immediate endocrine interest. It was concluded from the results of injecting phosphate solutions that the sodium-calcium ratio is the important factor in the production of tetany, with the exception of the gastric type. Gastric tetany is apparently due to an increase of the bicarbonate ion. No evidence has been found that the calcium-phosphorus ratio has any influence on the production of tetany.—F. S. H.

The effects of PROSTATE substance on the metamorphosis of the intestine of frog tadpoles. Hegner (R. W.) Am. J. Physiol. (Balt.), 1922, 61, 298-299.

Bull frog and green frog tadpoles were fed desiccated ram's prostate and Macht's observations were confirmed. The prostate contains something that stimulates the differentiation of the intestine of bull frog and green frog tadpoles.—T. C. B.

Further observations on the effects of the subcutaneous injections of splenic extract. Downs (A. W.) & Eddy (N. B.), Am. J. Physiol. (Balt.), 1922, 62, 242-247.

Confirmation of previous conclusions. Subcutaneous injections of "protein free" splenic extract causes a greater number of reticulated cells than normal in the circulating blood, the appearance of nucleated red corpuscles, and the resistance of the red corpuscles to extend over a wider range. The white corpuscles showed no change.—T. C. B.

The SPLEEN and digestion. Study II. The spleen and PANCREATIC secretion. Inlow (W. deP.), Am. J. M. Sc. (Phila.), 1922, 164, 29-44.

In this paper the author presents data concerning the pancreatic secretion, before and after splenectomy, on 2 dogs with permanent pancreatic fistulas secreting an inactive proteolytic juice, and on 2 similar nonsplenectomized dogs serving as controls. Removal of the spleen caused no constant change in the amount, enzyme content, or alkalinity of the pancreatic juice. The author concludes from a review of the literature and his own experimental inquiry that a definite trypsinogenic function of the spleen has not been demonstrated.—J. F.

The SPLEEN and digestion. Study III. The spleen in inanition; the effect of the removal of the external secretion of the PANCREAS on the spleen. Inlow (W. deP.), Am. J. M. Sc. (Phila.), 1922, 164, 173-188.

The data submitted in this paper seem to justify the conclusion that the spleen loses markedly in weight in inanition and out of

all proportion to the decrease in the body weight. The removal of the external function of the pancreas by ligation of its ducts or resection of a portion of the gland likewise leads to an excessive decrease in the size of the spleen. The shrinkage under these conditions, however, can be explained as due to the inanition and does not require the postulation of a specific pancreatic-splenic interrelationship.—J. F.

Increase of mitoses and of pyknoses in the THYMUS of the mouse after intraperitoneal injection of foreign serum (*L'onde de cinèses et l'onde de pynoses dans le thymus de la souris après injection intraperitonéale de sérum étranger*). Dustin (A. P.), *Compt. rend. Soc. de biol. (Par.)*, 1921, 85, 260-261.

The author studied the number of pyknoses and the number of mitoses which could be found in the thymus during the day following an intraperitoneal injection of aseptic foreign serum. The curve of pyknoses and that of mitoses were exactly inverse, and followed a definite law.—Physiol. Abst.

(THYMUS) Death after tonsillotomy due to status thymolymphaticus (*Fall von Exitus letalis nach Adenotomie bei Status thymolymphaticus*). Feuchtinger, *Wien. klin. Wchnschr.*, 1922, 35, 679.

In a child of 3 years respiration stopped immediately after operation. Artificial respiration was tried, tracheotomy was performed, and respiration began again. Next day death occurred due to paralysis of the heart. Postmortem examination showed a large thymus and enormous hypertrophy of both ventricles of the heart.

—J. K.

New views as to the morphology of the THYMUS gland and their bearing on the problem of the function of the THYMUS. Hammar (J. A.), *Upsala Läkaref. Förh.*, 1922, 27, 147-221.

Reprinted from *Endocrin.*, 5, 543-573; 731-760.—R. G. H.

A basic peptone-like compound in the THYMUS (*Ueber ein basischen pepitonähnlichen Körper in der Thymusdrüse*). Kiesel (A.), *Ztschr. f. physiol. Chem. (Berlin u. Leipz.)*, 1922, 120, 91-93.

Not of endocrine interest.—F. S. H.

(THYMUS) Sudden death in status thymico-lymphaticus (*Zur Erklärung der plötzlichen Todesfälle beim Status thymo-lymphaticus*). Ryser (H.), *Schweiz. med. Wchnschr. (Basel)*, 1921, 51, 554-557.

A brief review of the current theories on the subject. The author is inclined to place the blame upon an endocrine disturbance, though not necessarily of any one gland.—F. S. H.

The significance of the persistent THYMUS (*Die Bedeutung der Thymus persistens*). Yamanoi (S.), *Schweiz. med. Wchnschr.* (Basel), 1921, 51, 557-560.

Three hundred and three individuals who had died of acute grippe were examined for the presence of persistent thymus. The ages ranged from 25 to 50 years. Both sexes were investigated. There was found a persistent thymus in 24.4% of the group. The cases were not complicated with status thymico-lymphaticus. From the 25th to the 35th years the per cent of persistent thymi was 29.4; from the 36th to the 50th year it was 14.1. Because of the supposed correlation between thyroid and thymus, observations were also made on the former organ. There was found an enlarged thyroid in 73.9% of the group. In 77.0% of the cases where there was a persistent thymus there was also found an enlarged thyroid. Another smaller series showed 33.3% of persistent thymi.—F. S. H.

Phosphorus and ash content of the human THYMUS (*Zur la teneur en phosphore et en cendres du thymus*). Zunz (E.), *Compt. rend. Soc. de biol. (Par.)*, 1920, 83, 647-648; abstr., *Physiol. Abst.*, 1920, 5, 191.

Analyses were made of the thymus obtained from 44 men (age 19 to 34 years) killed in the war. The gland was first extracted with ether. The P ranged from 0.03 gm. to 0.31 gm. av. 0.1 gm., or from 2.62% to 4.50%, av. 3.57 %, of the dry thymus. The ash content ranged from 3.59% to 8.69%, av. 6.7%, of the dry gland. The ratio N:P was 2.80 to 6.61, av. 4.01. The per cent of ether extract tended to increase with the age of the subject. This age relationship did not exist for total solids (20.49%), total N (13.65% of the dry residue), P, and ash; the chemical composition of the gland did not vary with the age of the normal adult. Each gram of fresh thymus with its fat contained from 0.62 mgm. to 1.61 mgm., av. 1.09 mgm., of lipin P; if this lipin P exists only in the thymus proper, its amount would then range from 0.80 mgm. to 1.82 mgm., av. 1.32 mgm.; these values are intermediate between those for the liver and the kidney. In the adults studied, the entire thymus contained from 5.5 mgm. to 39.59 mgm., av. 17.47 mgm., of lipin P.—*Chem. Abst.*, 15, 2482.

(THYROID) The syndrome of Basedow's disease (*Le syndrome basedowien*). Achard (C.), *Progrès méd. (Par.)*, 1922, 37, 229-233; 265-268; 277-283.

A general discussion.—F. S. H.

(THYROID) The Basedowian syndrome (*Le syndrome basedowien*). Achard (C.), *Progrès méd. (Par.)*, 1922, 37, 241-244.

In this section of the general review of the disease under discussion there is taken up the general symptoms and the disturbances

of nutrition. The position is taken that at times discordant results of various observers are probably due to the complexity of the disorganization, which is not only attributable to the thyroid, but also to an insufficiency of several organs.—F. S. H.

(THYROID) The syndrome of Basedow's disease (Le syndrome basedowien). Achard (C.), *Progrès méd. (Par.)*, 1922, **37**, 289-292.

The last of a series of articles in which a general discussion of Basedow's disease has been reported. This one has to do with the therapeutics of the disorder. Hygiene, physiotherapy, opotherapy and x-ray or radium treatment are severally considered. Achard stresses the point that the cause of the disorder should be sought for and treated as well as the condition itself. Syphilis as a causative factor occurs in some cases; tuberculous thyroiditis is another; acute rheumatism another. The use of salicylates is indicated in Basedow's disease and particularly in disorders arising from the latter cause. Basedow's disease is not considered as a true entity since it is not distinguished by a specific cause peculiar to the disorder. In other words, Basedow's disease is an ensemble of symptoms, hence a syndrome. The principal disturbances of the syndrome are those arising from sympathetic excitation.—F. S. H.

THYROID therapy. Allison (R. G.), *Minnesota Med. (St. Paul)*, 1922, **5**, 404-409.

Of 27 cases of exophthalmic goiter without complications which were subjected to roentgen-ray treatment by Allison, 24 patients are well, both from the clinical and laboratory standpoint. The treatment has been complete for nearly 8 months. The remaining 3 cases came to operation. Of these 3, one was definitely improved before operation and the other 2 were normal a few months after operation. Of 6 cases of postoperative hyperthyroidism, which had relapsed, one showed a definite cure. The other 5 showed no improvement. Of 3 cases of thyrotoxic adenoma none showed any response to roentgen-ray therapy. The only patient operated on during an increasing basal metabolic rate died an operative death. No bad results or complications have occurred.—*J. Am. M. Ass.*, **79**, 682.

Studies on the mechanism of the increased metabolism in HYPERTHYROIDISM. Aub (J. C.), Bright (E. M.) & Uridil (J.), *Am. J. Physiol. (Balt.)*, 1922, **61**, 300-310.

Good evidence of the mechanism by which the active principle of the thyroid exerts its influence on metabolism is scanty and the present experiments were made to study further the increased heat production after thyroid injections, to see whether muscular movements, tonus, or adrenal secretion could be its cause. The usual methods were employed and the results charted. It is concluded that increased basal metabolism stimulated by thyroxin cannot be

explained by muscular activity, muscular fibrillation or increased muscle tonus. The adrenals are not essential. The findings support the theory that thyroxin stimulates resting cells directly to a higher level of combustion.—T. C. B.

Self observation of a case of migraine cured by **THYROID** treatment (Auto-observation d'un cas de migraine guéri par le traitement thyroïdien). Ballif (Charlotte), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 21-23.

The author takes occasion to record her cure of migraine by the ingestion of thyroid substance tablets to tolerance.—F. S. H.

Factors influencing the rate of mortality in surgery of the **THYROID** gland. Batchelor (J. M.), N. Orl. M. & S. J., 1922, 74, 468-473.

General discussion.—F. S. H.

THYROID therapy and prophylaxis of goiter with iodine (Zur Prophylaxis und Therapie des Kropfes mit Jod). Baumann (E.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 280-281.

A word of warning against the indiscriminate use of iodine therapy in every case of enlarged thyroid or so-called goiter since in some cases this condition is a hyperthyroidism which is certainly not helped by iodine administration. Such types of hypertrophied thyroid may occur in children also. The contention is made that the iodine tablets used for the school children contain altogether too much iodine.—F. S. H.

Glandular tests (considered with especial reference to functional disturbances of the **THYROID**) [L'épreuve des tests glandulaires (considérés surtout dans les maladies par trouble du fonctionnement thyroïdien)]. Bernard (S.) & Piédelière (M.), Progrès méd. (Par.), 1922, 37, 465-467.

Disturbances of function of the ductless glands are studied from the chemical standpoint (basal metabolism) and from the biologic standpoint (glandular tests). The present paper discusses the latter phase. A study was made of the action of adrenalin and pituitrin injections in patients with hyper- or hypo-function of the thyroid. The authors recognize that injection of these substances is not the equivalent of the secretion of the suprarenal and hypophysis. The method they used was to give subcutaneous injections of 0.05-0.15 of the extract of the posterior lobe of the pituitary or 1-3 c.cm. of a 1:1000 solution of adrenalin to the reclining patient and note the pulse rate and arterial tension and estimate the sugar output in patients given a meal of bread (100 gm.), milk (150 gm.) and sugar (50 gm). Reactions were usually produced 15-30 minutes after pituitary extract and 35-40 minutes after adrenalin. The sugar was commonly eliminated in the sixth to the ninth hour after injection. In patients with Basedow's disease adrenalin produced an intense and prolonged tachycardia, an increase of systolic pressure

and marked glycosuria, whereas in myxedematous patients similar injections produced little or no change. Injections of posterior lobe extract caused a definite slowing of the pulse, slow diminution of tension and a glycosuria in hyperthyroid patients and little or no modification of these in hypothyroid patients. Subjects with exophthalmic goiter react markedly to adrenalin and pituitrin, while those with myxedema react less than normal individuals to these injections. In hyperthyroidism the sympathetic and parasympathetic systems respond with a particular intensity to stimulation from adrenalin and pituitary extract, indicating a state of constant irritability of the vegetative nervous system.—C. E. N.

(**THYROID**) Goiter⁷ problem. Bickel (E. F.), Wisconsin M. J. (Milwaukee), 1922, 21, 87-90.

Reference verified from Quarterly Cumulative Index.

The blood chemistry of **THYROIDECTOMIZED** sheep. Bodansky (A.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 430-431.

Under controlled conditions it was found that the blood of thyroidectomized sheep differed from that of the normal. The sugar of the normal sheep ranged from 0.06 to 0.07 grams per 100 cc. of blood; the range for the thyroidless animals was from 0.04 to 0.05 grams. The non-protein nitrogen of the normal sheep was from 40 to 42 mg. per 100 cc. of blood; that of the thyroidless animals ranged from 28 to 32 mg.—F. S. H.

(**THYROID**) A case of familial angioneurotic edema complicated with **TETANY** (Ein Fall familiären angioneurotischen Oedems, kompliziert mit Tetanie). Bolten (G. C.), Deutsche Ztschr. f. Nervenhe. (Leipz.), 1919, 63, 360-367.

In a family of 12 there were 7 cases of angioneurotic edema. The particular patient concerning whom the report is made was a man of 40 years who suffered from tetany in addition to the usual accompaniments of the primary disorder. From the study of this case and others reported in the literature Bolten is of the opinion that edema of this type is not an individual disease so much as a consequence of a chronic intoxication due to congenital sympathetic hypotonia and hypothyroidism which cannot be dissociated from hypotonia. Such a condition obviously results in metabolic disturbances.—F. S. H.

Malignant adenopathy of bones of foot, probably of THYROID origin.

Brown (H. R.), J. Am. M. Ass. (Chicago), 1920, 75, 1780-1781.

A woman, aged 40, complained of throbbing pain in the leg and great toe. She felt "run down," without apparent cause. In 1911 she had had thyroidectomy for a tumor. Her health was good until May, 1916, when she complained of lumbago and a very tired feeling. Shoes worn at about this time were too small, and the toe was

pinched. Later the toe became inflamed and then "broke down," but finally formed granulation tissue and healed. In September, 1916, throbbing and dull pains were noticed in the toes of one foot. A roentgenogram at that time disclosed a distinct loss of bone substance of the toes, four of which were removed at two operations. For a brief interval there were no new developments; but after about a year and a half a swelling was noted on the dorsum of the foot and on the right ankle. The tumor mass was soft and painless to palpation and also to the needle. Radioscopy disclosed a definite loss of bone substance of the fibula and the fifth metatarsal bone, with little or no involvement of the joints. Blood, urine, and x-ray observations elsewhere, in addition to temperature, pulse, and respiratory examinations were negative. The pain in the leg and great toe continuing, a diagnosis of bone tumor of probable thyroid origin was made. Sections of the amputated great toe showed malignant, rapidly growing adenoma, although histologically it was impossible positively to state that the condition was of thyroid origin. Following this diagnosis, the leg was amputated at a point several inches above the tumor masses. One year after the amputation, there were no new developments. The tumor masses appear to have developed in the shaft of the bone in the cancellous tissue, and to have grown by peripheral development to a diameter twice that of the bone itself. As in none of the sections was it possible to find colloid deposits, it cannot positively be stated that the neoplasm had metastasized from the tumor of the thyroid reported to have been found in 1911.—I. B.

THYROTOXICOSIS. Buford (R. K.), *West Virg. M. J.*, 1921, 17, 100-105.

The author discussed the history, etiology, pathology and symptoms of thyrotoxicosis, and thinks we are a long way from a complete knowledge of the exact function of the thyroid and its effects—both good and ill—on the general physical economy. Crile's theory of likeness of the exophthalmic goiter to the symptoms caused by administration of epinephrin and thyroid extracts is interesting and he regards the blood picture as emphasized by Kocher very important and too much neglected in America. Thyrotoxicosis may be exogenous or endogenous. The deleterious substances may be normal metabolic products or the result of pathological processes. Disturbances of the thyroid offer a uniform series of symptoms. The number and severity of the symptoms are more or less dependent upon the amount of hypersecretion, the amount of this hypersecretion which is absorbed, the ability of the organism to neutralize or detoxicate the excessive secretion, and the stability or instability of the venous system. But better cooperation between the surgeon and the internist is needed before we can expect a great reduction in the present all too high rate of mortality, and a complete disappearance of the great numbers of chronic invalids who are at present the victims of thyrotoxicosis.—Author's Abst.

(**THYROID**) The characteristic electrocardiogram of the cretin sheep. Burlage (S. R.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 10, 425-427.

The electrocardiogram of the cretin sheep which had received no treatment differed definitely from the normal. The P and Q waves were either absent or just discernible. The R and T waves were very small, the latter being negative in all cases. In the case of the cretins which had received thyroxin the P waves were nearly normal in height and there were definite Q waves. The R waves were increased in height and the T waves were larger and positive in direction. The cretin treated with NaI in the food and the one treated with thyroxin subcutaneously showed the typical cretin graphs. Of the two lambs given thyroid in the food, one showed a graph slightly more normal than that of the untreated cretin and the other an almost normal picture. One pair of lambs was completely thyroidectomized when 23 weeks old. Subcutaneous treatment with thyroxin was begun 13 weeks later and continued for 15 weeks. Twenty-eight weeks later the electrocardiograms showed a distinct advance towards the normal from the cretin type.—F. S. H.

(**THYROID**) The treatment of exophthalmic goiter by radiations. Burrows (A) & Morrison (J. M. W.), *Proc. Roy. M. & Chir. Soc. (Lond.)*, 1920, 13, 132; abst., *Am. J. Roentgenol. (N. Y.)*, 1922, 9, 690-691.

The abstract cited gives the gist of the original article in considerable detail. In summarizing, the writers discuss the advantages and disadvantages of the medical and surgical treatment of exophthalmic goiter and conclude by saying that they do not think there is evidence that any treatment of exophthalmic goiter gives such safe, uniform and promising results as irradiation of the thyroid gland.—R. G. H.

The relation between **THYROTOXICOSIS** and tonsillar infection. Brown (L. E.), *Laryngoscope (St. Louis)*, 1922, 32, 590-607.

Report of the results of a questionnaire. The majority believe that goiter is of toxic origin and that the tonsil is no more likely to be the focus of infection than any other location.—H. W.

Acceleration of growth and regression of organ-hypertrophy in young rats after cessation of **THYROID** feeding. The production of tetany in rats by thyroid feeding. Cameron (A. T.) & Carmichael (J.), *Tr. Roy. Soc. Canada (Ottawa)*, 1922, 16, Sect. V, 57-70.

The various body organs, heart, kidneys, adrenals, liver, etc., which hypertrophy in young white rats as a result of feeding thyroid gland, regain normal size within a few weeks after cessation of such treatment (confirming Hewitt, *Endocrinol.*, 5, 148), while at the same time there is an acceleration of growth which in most cases

completely compensates for the retardation produced by thyroid feeding. This is attributed to the hypertrophy of the essential organs, the cessation of the thyroxin stimulus, and the subnormal thyroids of the treated animals. Of 72 young rats fed thyroid in this and previous series of experiments 10 developed definite tetany; 4 of these recovered. The immediate cause of such tetany is attributed to the rapid breathing invariably present in these cases.

—A. T. C.

(**THYROID**) Basal metabolism as aid in diagnosis of toxic goiters. Cannon (J. H.), J. South Car. M. Ass. (Greenville), 1922, 18, 224-226.

Reference verified from Quarterly Cumulative Index.

Dementia praecox and THYROID (*Deméncé précoce et phénomènes thyroïdiens*). Chernbach (M.) & Vasilu (D.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 77.

Case presentation of a young man of 22 years of pathogenic heredity (mental). The patient presented schizophrenic symptoms accompanied by exophthalmia and thyroid hypertrophy. No tachycardia was present.—F. S. H.

THYROID glands. Clark (H. C.), Kentucky M. J. (Bowling Green), 1922, 20, 547-549.

Some observations on the **THYROID gland.** Cobb (I. G.), N. York M. J. [etc.], 1922, 115, 377-382.

From a review of the literature and personal observations the author concludes that goiter is often the result of toxemia. Thyroid therapy is advised in combating toxemia for the reason that the thyroid hypertrophies in its unsuccessful attempt of detoxicating the body.—H. W.

(**THYROID**) Control of so-called **HYPERTHYROIDISM** by digitalis and water. Crile (G. W.), N. York M. J. [etc.], 1922, 115, 376-377.

The cycles of cardiac dilation, tachycardia, fever, nausea and vomiting, restlessness, flushed face, occasional diarrhoea and acetone breath observed in cases of exophthalmic goiter and believed to be caused by an acute overactivity of the thyroid, according to Crile, are simply signs of an acute intracellular acidosis. The acidosis produced from the accumulation of acid products results from the excessive metabolism of exophthalmic goiter. In such cases every organ is overactive, hence it follows that the body requires an increased amount of water in circulation to carry off acid waste products. When the heart is no longer able to circulate water and oxygen to the brain and liver—"motor organs"—there results an intracellular

accumulation of acids. From this reasoning Crile has adapted the use of water and digitalis in both the preoperative preparation and postoperative management of exophthalmic goiter patients. By this means of treatment the mortality rate of 1,869 thyroid operations, including 1,069 for exophthalmic goiter, was 1.3 per cent (25 deaths). The mortality rate of 783 ligations was 0.73 per cent (6 deaths). Technique is given.—H. W.

Contribution to the histophysiology of the **THYROID** body (Contribution à l'histophysiologie du corps thyroïde). Courrier (R.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 869-870.

Utterström finds an augmentation of colloid in the vesicles after hyperthyroidization, while Jensen obtained opposite results in the tadpole. The author fed young cats 0.5 gm. fresh thyroid for 4 months, and found more colloid in the thyroid vesicles of the experimental animals than in the controls from the same litter. Double secretory polarity which is described by Cowdry is discussed and it is suggested that the cats fed on thyroid have their "milieu interieur" saturated with thyroid products which serve to maintain metabolism, while normal hormones are rendered useless. Thyroid cells are polarized only toward the vesicle and place in reserve the products which have not been utilized in the organism.—T. C. B.

Mechanism of the therapeutic action of iodine in **HYPERTHYROID** conditions (Mecanismo de la acción terapéutica del yoduro en los estados de hipertiroidismo). Delgado (H. F.), La Crón. méd. (Lima), 1919, 36, 155-157.

A speculative discussion.—F. S. H.

(**THYROID**) Surgical treatment of goiter. Epps (C. B.), J. South Car. M. Ass. (Greenville), 1922, 18, 230-233.

Reference verified from Quarterly Cumulative Index.

(**THYROID**) Riedel's "iron-like" goiter (Zur Kenntnis der Riedel-schen eisenharten Struma). Erkes, Deutsche med. Wchnschr. (Berl.), 1922, 48, 929.

The author considers this goiter as an inflammation of the thyroid. No details are given.—J. K.

(**THYROID**) Goiter: from the standpoint of the clinician. Ervin (A. B.), Penn. M. J. (Harrisburg), 1922, 25, 760-767.

This article is a concise review of the physiology of the thyroid, and the classification and treatment of goiter from the surgeon's point of view. Ervin divides goiter into three types: (1) colloid of adolescence; (2) exophthalmic, and (3) adenoma. Colloid goiter of adolescence is preventable and usually curable by proper iodine administration according to Marine and others, but in this author's ex

perience in a small series of colloid goiter, the administration of potassium iodide resulted in no appreciable reduction in the size of the mass. Exophthalmic goiter constituted 14% of the 530 cases of the author's series. The average age was 33 years, with an average duration of the illness of $3\frac{1}{2}$ years. Though basal metabolism determinations are useful, the skilled diagnostician does not find them essential. The author rightfully states that "the best results are obtained by the man who goes about the treatment of these patients with an open mind, willing to accept whatever may be of the most service to his patient," yet surgery is strongly insisted upon as the treatment holding forth the greatest promise of cure. The treatment of thyroid adenomata, whether simple or toxic, is essentially surgical. It is well for the laity to be informed of the dangers of postponing treatment of an adenoma, as a large percentage develop toxic symptoms so insidiously that marked damage to vital structures may occur prior to final diagnosis, rendering operation more hazardous. Suppurative thyroiditis occurred twice in the author's series; one patient was a girl of 13, the other a woman of 65. Tuberculosis and syphilis of the thyroid are rare. Thyroid carcinoma occurred in 1% of the author's cases.—I. B.

The adrenalin test in the diagnosis of **HYPERTHYROIDISM** (La prueba de la adrenalina en el diagnóstico del hipertiroidismo). Escudero (P.), *Semana méd.* (Buenos Aires), 1921, 28, 116-117.

The author's investigation of the value of the adrenalin test in the diagnosis of hyperthyroidism comprises a study of 180 cases. He found that the reaction is not specific of hyperthyroidism. In patients negative with thyroidin, the adrenaline test was positive in 34%. In patients positive with thyroidin, the adrenalin test was negative in 20%. Experimental hyperthyroidism produced by the ingestion of thyroid gland merely reduces the number of instances negative to adrenalin, but does not eliminate them. These facts speak against the specificity of the adrenalin reaction in the diagnosis of hyperthyroidism.—I. B.

Recent metabolic findings in the diagnosis and treatment of diseases of the **THYROID** gland. Fahrni (G. S.), *Canad. M. Ass. J.*, 1922, 12, 386-389.

The material for this paper is prepared from personal observation of a series of cases presenting evidence suggestive of disturbed thyroid function. The writer endeavors to show how the careful estimation of basal metabolism strikes at the very heart of diagnosis. This applies particularly in differentiating hyperthyroidism from psychoneuroses, essential hypertension, neurocirculatory asthenia and certain other pathological conditions, the clinical appearances of which are frequently confused with that of disordered function of the thyroid gland. The help given by metabolism estimation in both surgical and medical management of cases of hyper-

A case of **THYROID-OVARY** psychosis cured by thyroidectomy and ovarian opotherapy (Sur un cas de psychose thyro-ovarienne guéri par thyroïdectomie et opothérapie ovarienne). Goldner (J.) & Gheorghiu (V.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 11-17.

The title tells the story and is taken by the authors to prove the important rôle of thyroid hyperfunction in mental disorders.

—F. S. H.

Administration of **THYROID** gland in hydrocephalus. Gray (J. P.), Lancet (Lond.), 1922, ii, 177.

This is a brief clinical note describing a case of extreme hydrocephalus in an infant treated successfully with thyroid extract. The hydrocephalus developed at the age of 6 months. When other therapeutic measures had failed and the patient was in an almost hopeless condition, thyroid extract, $\frac{1}{2}$ to 1 grain per day, caused prompt improvement and, according to the author, complete cure within 8 months.—I. M.

(**THYROID**) Suppurative strumitis during puerperal infection (Les strumites suppurées au cours de l'infection puerpérale). Grimault (L.) & Brino (H.), Gynéc. et Obst. Rev. (Par.), 1922, 6, 167-175.

Report of a case of suppurative thyroiditis in puerperal infection and review of the literature. It is shown that the disturbance usually arises in a pre-existing goiter. The symptoms are essentially those of thyroiditis. Prognosis is grave. The mortality recorded is 11%. Surgical interference is indicated.—F. S. H.

The influence of restricted diet and **THYROID** feeding on the tadpoles (Unzureichende Ernährung und Hormonwirkung. II. Der Einfluss unzureichender Ernährung und Schilddrüsenfütterung auf den Sauerstoffverbrauch der Larven von Rana temporaria). Groebbels (F.), Ztschr. f. Biol. (München. u. Leipz.), 1922, 156-168.

The metabolism and the consumption of O_2 of tadpoles fed insufficiently and lagging in their growth is relatively greater than of normal animals of the same age. In normally fed animals given thyroid in addition the consumption of O_2 is increased. With diminishing body weight it increased both absolutely and relatively. Animals with insufficient food plus thyroid consume relatively less O_2 . Thyroid effects may thus be influenced by nutritional conditions.

—Physiol. Abst., 7, 312.

(**THYROID**) The relation of water to the production of goiter. Guittard (V. D.), Kentucky M. J. (Bowling Green), 1922, 20, 612-615.

From a review of the literature the author concludes that goiter is a water-borne disease occurring in areas of iodine deficiency.

—H. W.

Toxic adenoma of **THYROID** gland. Gunby (P. C.), Texas State J. M. (Ft. Worth), 1922, 18, 204.

The writer reviews Plummer's differentiation of exophthalmic goiter and toxic adenomas of the thyroid but does not emphasize the necessity for removal of adenomas before toxic symptoms develop. He states that ligation is ineffective in adenomas, that radium and x-ray are usually of only temporary benefit.—C. R.

Studies of the **THYROID** apparatus. VII. A differential effect of **THYRO-PARATHYROIDECTOMY** and **PARATHYROIDECTOMY** on the incisor teeth of the albino rat. Hammett (F. S.), Am. J. Physiol. (Balt.), 1922, 62, 197-201.

Of 20 rats with the thyroids and parathyroids removed, only one, or 5%, developed dental defects, while of 26 rats with the parathyroids alone removed, twenty, or 76.9%, developed defects of the teeth. It is suggested that as the function of the thyroid is stimulative, "and the function of the parathyroids is inhibitive of a certain phase of nitrogenous metabolism, the by-products of which may give rise to general stimulation when not taken care of by the parathyroid secretion," the result may be a disturbance of calcium metabolism, resulting in dental defects, when the parathyroids are removed.—T. C. B.

(**THYROID**) Surgical treatment of exophthalmic goiter. Hill (J. H.), Texas State J. M. (Ft. Worth), 1922, 18, 205.

Hill believes that exophthalmic goiter is a surgical, not a medical disease, that many cases are operated upon late because of discouraging advice of physicians. He believes that those who persist in treating these cases medically until they become poor surgical risks, only referring them to the surgeon as a last resort, do their patient great injustice.—C. R.

Metastasis of a cancer of the stomach in the **THYROID**; growth into the larynx (Schilddrüsenmetastase eines Magenkarzinoms mit Einwachsen in den Kehlkopf). Hofer, Wien. klin. Wchnschr., 1922, 35, 612.

No details are given.—J. K.

(**THYROID**) Some observations on the treatment of **HYPERTHYROIDISM** with x-rays. Holmes (G. W.), Am. J. Roentgenol. (N. Y.), 1921, 8, 730-740.

The results of observations of x-ray therapy in a series of cases studied at the Massachusetts General Hospital are presented, and the importance of the cooperation of the clinician, surgeon and roentgenologist is emphasized. Colloid, cystic and simple goiters are not amenable to the x-rays. Malignant goiter requires immediate operation followed by postoperative raying and if surgery is for

some reason contra-indicated, roentgenization alone may result in temporary benefit. Toxic adenomata respond readily to x-rays, but surgery yields more prompt relief. Non-toxic adenomata may yield to roentgenization, but as a rule these cases are kept under observation or treated surgically. Exophthalmic goiter responds satisfactorily to roentgenotherapy. In very toxic cases, a period of rest precedes the institution of x-ray treatment. Eight case histories are reviewed exhibiting the merits as well as the faults of x-ray therapy. Holmes advises the following technic. The dosage varies with the type of case. In early cases an 8-inch target-skin distance is used; 4 mm. aluminum filter with 8 inch parallel spark gap between points is employed. Lately, he has been using a 10 inch and in some cases a 16 inch skin distance, thus increasing the amount of radiation to the gland with a proportional diminution of radiation to the skin. In most cases three exposure areas are used, one on each side of the neck and one over the thymus region. In some instances where a 16 inch distance is used, one single exposure is given in the midline, including the thyroid and upper thymus regions. In certain cases, 5 areas of exposure are used, one over each side of the neck, one over the thymus, and two over the back of the neck. The time interval between treatments is usually .3 weeks, but in some instances it is 2 weeks. The author believes that a shortening of the interval between treatments is preferable to an increase of dosage when a maximum effect of radiation is desirable. Results of treatment are checked up by basal metabolism observations. The question of skin tolerance must always be borne in mind, and erythema is rarely necessary. There is always a possibility of such injury to the skin as atrophy and telangiectasis; these can be avoided by keeping well below the erythema dose. In cases responding favorably to treatment, there is at first an improvement in the nervous symptoms, observable within 3 weeks; at the end of 6 weeks a drop in pulse rate and metabolism is seen, but in many instances clinical response is more gradual. The metabolism and pulse rate may return to normal after 6 or 7 treatments have been given, corresponding to a period of 4 to 6 months. Weight is gradually increased, goiter is reduced, and exophthalmos, if present, is relieved. In cases which do not yield to x-rays, rest is insisted upon or surgery resorted to after the fifth or sixth treatment. Cases having received treatments over periods of from one to two years have been found more difficult at operation. Myxedema may result from too heavy or too prolonged radiation, or it may develop several years after radiation because of contracting connective tissue. It must be borne in mind, however, that a patient with hyperthyroidism may develop myxedema under any treatment and even spontaneously.—I. B.

Some phases of **DYSTHYROIDISM**. Howard (C. P.), *Canad. M. Ass. J.*, 1922, 12, 606-609.

It is held that a normal basal metabolic rate can at most signify an absence of a marked thyroid toxicity. The author differs with

Plummer and Boothby, who "insist that the term 'hyperthyroidism' implies necessarily an increased metabolic rate." A series of 12 cases is cited to prove his point, the clinical symptoms being summarized in such a way that a clear picture of dysthyroidism is presented and all in the absence of an increase in the basal metabolic rate. In 2 cases the superior thyroid arteries were ligated. "In the future we shall unhesitatingly urge a partial lobectomy as the procedure of choice."—J. H.

Ligation operations in the treatment of diseases of the THYROID gland. Hume (W. I.), Kentucky M. J. (Bowling Green), 1922, 20, 344-348.

It is of the greatest importance to reduce thyroid activity, especially in the handling of exophthalmic goiter. Ligation of the superior poles of the gland, though temporary in its effect, and not without a mortality of its own, is at present, perhaps, the safest measure of affecting a reduction in the activity of the gland.—H. W.

Three years of THYROID observations (Drei Jahre Schilddrüsenmessungen). Hunziker (H.), Schweiz. med. Wchnschr. (Basel), 1920, 50, 1009-1014.

Studies were made of the influence of iodine administration to children on the size of the thyroid gland as measured by the circumference of the neck in two positions, upright and flexed. Apparently the ingestion of iodine tends to result in a thyroid of smaller size in many cases.—F. S. H.

Roentgen ray therapy of HYPERTHYROIDISM. Jenkins (I. W.), Texas State J. M. (Ft. Worth), 1922, 18, 213.

Jenkins states that radio-therapy is effective only in exophthalmic goiter and toxic adenoma, and in the latter believes that surgery is perhaps advisable, as the risk is slight and recovery quicker. In exophthalmic cases and cases in which the thymus is involved, he commends radio-therapy even though surgery is to follow.—C. R.

Basal metabolism determination and its technical difficulties. Jones (H. M.), J. Lab. & Clin. M. (St. Louis), 1922, 7, 191-198.

A thorough knowledge of the basic principles common to all methods and devices employed in basal metabolism determination is the outstanding essential to success. The result of a given determination should be the algebraic sum of the plus and minus errors from at least three widely different sources, namely: (1) the test subject, who, though in normal health may have a metabolic rate varying several per cent from his expected rate, and who may co-operate irregularly or not at all in the performance of the test; (2) the technician, who must execute many details and observations besides those pertaining directly to the manipulation of the instrument; and (3) the apparatus itself, which may introduce error, perhaps consistent, perhaps variable, because of certain of its mechan-

ical defects unknown to the operator. In 1920, the author, while testing out his own apparatus, made comparisons of its results with those of apparatus of other makes in nearby hospitals and laboratories, and it was then that he observed the most noteworthy, not to say startling, errors committed in metabolic determination. For example, in a normal test subject, the metabolic rate was seen to vary from -17 to $+90$ through various errors, all of which were discovered to be classifiable in the above mentioned groups. On subsequent occasions the author found this deplorable state of affairs to exist throughout all parts of the country, and aptly states that "any technician or clinician who feels that his own results are an exception to this, should see to his own technic in securing normal readings on known normal subjects before offering challenge to the proposition." Since the subject, the technician and the apparatus are severally responsible for the errors encountered in these tests, the beginner should start with one of these factors as a known and relatively fixed quantity, namely, a cooperative test subject in normal health. In this way, the other two sources of error may then be reduced to known quantities, and in turn eliminated. On over 100 different occasions, Jones witnessed the beginning technic of over 100 clinicians or their technicians. Not one of them, during their first attempts, came anywhere near the proper handling of the apparatus or the subject during the period of testing. On one occasion the technician reports a $+8$ per cent reading on a suspected hyperthyroid patient. The subject was dismissed as a "neuro." Four months later, the physician, convinced that some error in the test had been made, ordered the technician to make a second test. This time the reading was $+58$ per cent. Soon it was discovered that the rate as determined two months previously should have been reported as $+35$ per cent instead of $+8$ per cent. Now, however, the patient was so much worse that radical operation performed two weeks later eventuated fatally. On another occasion Jones observed a patient nearly asphyxiated during the course of the test because a tank of gas supposedly oxygen but containing nitrous oxide was used. Jones emphasizes the importance of the technician's ability to secure normal readings on known normal subjects, and unless the operator is equal to this task, results with suspected pathological cases are unreliable. It is not enough to imagine that the apparatus is accurate if it will give a plus reading on a known hyperthyroid patient, since an inaccurate apparatus may still give the desired plus reading. Having learned the technic on normal subjects, the tests may be made in a series of pathological cases. If, in the meanwhile, a mechanical defect giving rise to an error is suspected, the operator must endeavor to eliminate it by another series of observations on persons known to be normal. The technician's desire to learn, coupled with duplicate determinations and appropriate controls, are essential in rendering basal metabolism observations reliable.—I. B.

(THYROID) A clinical classification of **HYPERTHYROIDISM**—exophthalmic goiter. Johnson (C. C.), Nebraska M. J. (Omaha), 1921, 6, 70-72.

A discussion of the symptomatology and treatment of goiter based upon the author's conception of a working clinical classification of diseases of the thyroid, which is as follows: A. Primary, (a) fulminating, (b) acute, (c) subacute; B. Secondary, (a) typical, (1) adolescent, (2) mature, (b) atypical, (1) mature; C. Neurotic, (a) adolescent, (b) adult. Primary goiters are exophthalmic in type, the pathology of which closely resembles malignancy. In the fulminating form the expectant treatment is indicated, as surgery hastens death. In the acute and subacute forms close observation, tact, a reduction of psychic trauma with sedative and supportive measures should dominate treatment. When the weight is restored to normal, active treatment should be considered. In the management of exophthalmic goiter conservatism is the rational attitude, and surgery should never be employed except as an emergency measure. Secondary goiters are non-exophthalmic in type, of varying pathology. In the adolescent form the removal of discoverable infectious foci, rest, hygiene, medication, with or without x-rays yield results, and when there are cystic or adenomatous changes, surgery is indicated. Mature goiters are potentially treacherous, as they are capable of becoming toxic or malignant in nature; hence surgery is the treatment of choice. The atypical goiter is often overlooked as the symptoms are mild and at a distance from the thyroid. X-ray treatment (plus medicinal measures) yields good results, and if cystic or adenomatous conditions exist, surgery is indicated. Neurotic forms of goiter present hypertrophic adenomatous, round cell infiltration with or without colloidal or cystic changes. Mental symptoms in the nature of hysteria, precocity, or a psychosis are apt to predominate. Exophthalmos is absent, but tremor, tachycardia and enlarged thyroid are common. These patients do poorly under any treatment. Hospitalization with the services of a neurologist is advised. Both x-rays and surgery are disappointing in the treatment of this type.—I. B.

Basal metabolic rating as a basis of classification and treatment of THYROID conditions. Jones (H. P.), N. Orl. M. & S. J., 1922, 75, 28-32.

A short paper in which thyroid conditions are divided into 3 types, depending upon whether there be minus, normal, or plus basal metabolism. Basal metabolism observations are the only reliable guide in the diagnosis of thyroid affections and they assist in the indication of the mode of treatment to be adopted in a given case.

—I. B.

(THYROID, DIABETES) Observations on the excretion of sugar in the urine in health and disease. Kast (L.) & Croll (H. M.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, 19, 84.

In hyperthyroidism the average range of sugar excretion was between 0.46 and 0.98 grams. In one case of hypothyroidism the average excretion was 0.40 grams. In 4 normal adults the average daily amount was between 0.59 and 1.14 grams. In diabetes alone is there an increase.—F. S. H.

(THYROID) Adiposis dolorosa (Ueber Adipositas dolorosa). Kaufman (F.), Schweiz. Arch. f. Neurol. u. Psychiat. (Zürich), 1921, 9, 108-124.

Report of two cases of adiposis dolorosa in which the idea of thyroid or pituitary participation was not tenable. Beneficial results were obtained from the ingestion of thyroïdin to tolerance. The improvement is attributed to general metabolic stimulation.—F. S. H.

THYROID preparation. Kendall (E. C.), U. S. Patent 1,392,767, Oct. 4, Chem. Abst. (Easton, Pa.), 1922, 16, 465-466.

A description of the method of separating active thyroid preparations from thyroid glands.—F. S. H.

THYROID preparation. Kendall (E. C.), U. S. Patent 1,392,768, Oct. 4, Chem. Abst. (Easton, Pa.), 1922, 16, 466.

A modification of the procedure included in the foregoing patent.—F. S. H.

Anaphylaxis in thyroidectomized animals fed with THYROID (Anaphylaxie chez les animaux ethyroïdes nouris avec de la thyroïde). Képinow (L.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 409-411.

It has been shown that thyroidectomized animals, after sensitizing injections of horse serum, do not contain in their blood the substance necessary to confer passive anaphylaxis on other animals, either operated upon or not. The present report attempts to answer the question whether the feeding of thyroid to such animals will restore this substance. Of 10 thyroidectomized guinea pigs, 7 were fed dried thyroid, while 3 were kept as controls. Eighteen days after the sensitizing injections all were given an intoxicating dose. The 7 that were fed thyroid died of typical anaphylaxis, while the controls showed no symptoms. The blood of thyroidectomized animals that have been sensitized to horse serum, and at the same time fed dried thyroid, will confer a passive anaphylaxis when injected into other animals.—T. C. B.

The rôle of the THYROID gland in anaphylaxis (Contribution à la question du rôle de la glande thyroïde dans le phénomène d'anaphylaxie). Képinow (L.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 494-495.

A short discussion of Kepinow's theory, that the thyroid interferes with the elaboration of substances necessary for the production of anaphylaxis.—T. C. B.

THYROID gland and anaphylaxis (Glande thyroïde et anaphylaxie).
Képinow (L.) & Lanzenberg (A.), *Compt. rend. Soc. de biol.*
(Par.), 1922, 86, 906-908.

In a previous note (see *Endocrin.*, 1922, 6, 579), it has been shown that thyroidectomized animals do not suffer from anaphylactic shock. The present paper deals with passive anaphylaxis. Horse serum was the sensitizer; rabbits and guinea pigs were used. Normal guinea pigs, when injected with the blood of sensitized guinea pigs, suffered from anaphylactic shock. Thyroidectomized guinea pigs suffered anaphylaxis when injected with the blood of sensitized guinea pigs. Normal guinea pigs injected with the blood of thyroidectomized guinea pigs previously treated with horse serum gave no symptoms. The same is true for the blood of rabbits injected into guinea pigs. Thyroidectomized animals can be sensitized passively, and present the phenomena of anaphylactic shock when injected with an intoxicating dose, but their blood is lacking in some substance necessary to sensitize non-operated animals.—T. C. B.

Observations on the cardiovascular system in THYROID diseases.
Kerr (W. J.) & Hensel (G. C.), *Calif. State J. M.* (San Fran.),
1922, 20, 306-309.

From a consideration of 181 goiters, 123 of which were classified as adenomatous and 58 as hyperplastic, the authors conclude that cardiovascular changes are progressive in nature. The cardiac signs and symptoms in toxic adenomas and hyperplasias differ only with the degree of toxicity. Cardiac irregularities are common. Auricular fibrillation, usually paroxysmal in type, occurs in about 33 per cent of all toxic cases. Treatment depends upon the degree of the thyrotoxicosis. Digitalis is of great value in controlling auricular fibrillation and should be continued over long periods of time.
—H. W.

(THYROID) The relation between the blood and the organs (*Beziehungen zwischen Blut und Organen*). Kottmann (K.), *Schweiz. med. Wehnschr.* (Basel), 1920, 50, 1060-1064.

The author reports that there is a difference in the ability of serum from patients with various types of thyroid disturbances to reduce colloidal silver iodide on the addition of hydroquinone. Serum from Basedow's disease apparently causes a marked retardation of the reduction. This is attributed to an extremely fine state of division of the iodized colloid. On the other hand, serum from goitrous patients accelerates the reduction. There is a correlation between these findings and the histological appearance of the thyroid in the two disorders. In the one the colloid is thin; in the other, concentrated. On the basis of these observations a theory is built up which as yet needs other evidence for substantiation. The relation of parathyroid function to guanidine metabolism is discussed.
—F. S. H.

(**THYROID**) Basal metabolism in Basedow's disease (*Métabolisme basal chez les Basedowiens*). Labbé (M.) & Stévenin (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 1012-1014.

An examination of 8 cases of typical Basedow's disease, 11 cases of "Basedow fruste," 6 cases of simple goiter and 1 case of unilateral exophthalmos confirms the results of others. In the typical cases the metabolism is constantly and strongly augmented (average 66%). In the "formes fruste" there is also augmentation (average 51%). In simple goiter metabolism is often normal, but may be a little augmented. The measure of metabolism is useful in the diagnosis and prognosis of Basedow's disease.—T. C. B.

(**THYROID**) Induced hyperglycemia in Basedow's disease (*L'hyperglycémie provoquée chez les Basedowiens*). Labbé (M.), Labbé (H.) & Nepveux (F.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 1014-1015.

The test of induced hyperglycemia and the measure of basal metabolism are two physiological procedures that have a great value in the diagnosis of the hyperthyroid state.—T. C. B.

Basal metabolism as an index of treatment in diseases of the **THYROID**. Lahey (F. H.) & Jordan (S. M.), *Boston M. & S. J.*, 1921, **184**, 348-358.

Report of 304 tests on 135 individuals, 25 of whom were normal and 110 with thyroid disease. Metabolism determinations are of great value in determining the degree of thyroid function following operative procedures.—H. W.

Psychosis of **THYROID** origin (*Les psychoses thyroïdiennes*). Laignel-Lavastine (M.), *Progrès méd. (Par.)*, 1922, **37**, 158-163.

A theoretical, philosophical discussion of the frequent relationship found to exist between psychoses and thyroid disturbances leading to the conclusion that the dysthymias of thyroid origin depend more upon the psychic entity than upon the chemical cosmos.

—F. S. H.

(**THYROID**) Diagnosis and treatment of toxic goiters. Lemmon (C. J.), *J. South Car. M. Ass. (Greenville)*, 1922, **18**, 226-230.

Reference verified from Quarterly Cumulative Index.

Anaphylaxis, colloidoclasia, **THYROID** body (*Anaphylaxie, colloidoclasie, corps thyroïd*). Lévi (L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **86**, 1083-1084.

The author points out that in 1912, without furnishing experimental proof, he discussed the rôle of the thyroid in the problem of anaphylaxis.—T. C. B.

(**THYROID**) A study of exophthalmic goiter and the involuntary nervous system. **VIII. A clinical and laboratory study of the in-**

voluntary nervous system. Lieb (C. C.), Hyman (H. T.) & Kessel (L.), J. Am. M. Ass. (Chicago), 1922, 79, 1099-1101.

According to the authors the manifestations of exophthalmic goiter may be divided into the metabolic disturbance measured by the basal metabolism, and the sympathomimetic symptoms (tachycardia, exophthalmos, polyrrhea, sweating, etc.). To a clinical association of sympathomimetic symptoms and normal basal metabolism the term "autonomic imbalance" is applied. In 86 cases of this latter type the commonest symptom was lability of pulse rate, thyroid enlargement being second in frequency. In 84% both were present. In all the basal metabolism was normal. In attempting to discover a pathognomonic clinical test the response to atropin and epinephrin was studied. In 80 normal subjects 33% reacted to epinephrin and 25% to atropin. In a few cases of autonomic imbalance and 50 cases of exophthalmic goiter the intensity of drug reactions did not parallel the severity of the symptoms, although only 6% failed to react to one or the other drug. The authors are convinced that the epinephrin reaction (Goetsch) is independent not only of the normal, but also of the hyperplastic thyroid gland. Results of animal experiments in which the response of the pithed cat to repeated injection of similar doses of epinephrin was investigated are to be published later. This research led them to conclude that the epinephrin sensitization is independent of the ductless glands and is not a specific hormone effect, but is a physico-chemical change involving the myoneural junctions of the thoracico-lumbar system. It seems unwise to call exophthalmic goiter and autonomic imbalance endocrine disorders. The relationship between autonomic imbalance and exophthalmic goiter is not clear, but the former often precedes the latter and transition stages are seen.—W. M. A.

Pathological classification of THYROID gland diseases with radium treatment in toxic goiter. Loucks (R. E.), Am. J. Roentgenol. (N. Y.), 1921, 8, 755-765.

This article is an exposition of the author's conception of the pathological classification of goiter, with mention of Plummer's clinical classification, and does not lend itself to detailed abstracting. The symptoms of toxic adenoma and of exophthalmic goiter are outlined and a few clinical features differentiating the two are mentioned. Among the symptoms of bad prognosis in exophthalmic goiter are exophthalmos for two or more years, edema of the extremities, auricular fibrillation, hypertension, marked emaciation, high metabolic rate, persistent diarrhea, cerebral symptoms, acidosis and a positive Wassermann reaction. With regard to treatment, it is stated that if after two weeks of hygienic, dietetic and medicinal measures, there are still evidences of thyroid toxemia, a choice between surgery, x-ray and radium must be made. Surgery in toxic goiter is not advocated. Radium is the treatment of choice because

it is portable, less exciting, easily controlled, does not produce sudden toxemia, and the results are more promising than with x-rays. Radium treatment must be supplemented with the usual medicinal treatment. At least 100 mgm. of radium are used in four tubes, each screened in 1 mm. of brass and 1 mm. gum rubber. The screened tubes are placed on a gauze pad 2 cm. thick to get distance and protect the skin. Two or three ports are exposed over the thyroid, depending upon the size of the gland, size of the pad, and the amount of radium used. The time of exposure is from 8 to 10 hours over each part.—I. B.

(THYROID) The world's supply of iodine in relation to the prevention of goiter. McClendon (J. F.), Science (N. Y.), 1922, n. s. 56, 269-270.

An analysis of sea water obtained at Santa Monica, Cal., showed 0.05 mgm. of iodine per liter. Water taken from the Great Salt Lake, Utah, contained 40% more iodine than sea water, but the chlorine was 500% greater. This indicates that weathering of both igneous and sedimentary rocks gives very little iodine. Thus inland waters would contain very little of this element. It is suggested that powdered kelp be used with food to furnish iodine. Table salt could be made from sea water, thus furnishing iodine.—F. A. H.

(THYROID) Feeble-minded and backward children. McCready (E. B.), Internat. Clin. (Phila.), 1922, 3, 118-162.

A good historical and clinical discussion on the subject of mentally deficient children, with brief mention of cretinism, and of endocrine implications in treatment. While opotherapy frequently yields brilliant results in cases of undoubted endocrinopathy, the use of glandular products as a panacea or specific in the management of defectives generally will meet with disappointment.—I. B.

Helpful technique for operations on the THYROID gland. Mc-Nerthney (J. B.), Northwest Med. (Seattle), 1922, 21, 189-191.

A goiter clamp, self-retracting, is described obviating the maladroit careless mauling and hauling of an inexperienced assistant. Directions are given for accurate local anaesthesia in thyroid surgery.
—H. L.

The emotional factor in the pathogenesis of HYPERTHYROIDISM (Le facteur émotionnel dans la pathogénie des états hyperthyroïdiens). Marañón (G.), Ann. de méd. (Par.), 1921, 60, 81-95.

After citing some 48 cases and giving a brief review of the prevalent opinions Marañón concludes that the emotions have an undoubted influence in the pathogenesis of Basedow's disease and other hyperthyroid conditions. In the majority of cases emotion is effective in individuals predisposed to hyperthyroidism. In the minority of cases emotion acts as the primary cause.—F. S. H.

(THYROID) Affections of the ear in CRETINISM (*Les affections de l'oreille dans le crétinisme*). Mager (F. D.), 10th Cong. internat. d'otol. (Par.), 1922, July 19-22; abst., *Presse méd. (Par.)*, 1922, 30, 703-704.

The author first brings out the clinical symptoms of endemic cretinism, especially from the point of view of lesions of the ear. Aside from recognized cretin deafness with signs of degeneracy like dwarfism, defective intelligence, goiter, and cutaneous alterations, there are also other forms of deafness. In these last cases isolated signs of degeneracy are often more or less marked. With the aid of a series of microscopic sections Mager points out the anatomical and microscopical changes in the ear which he has found lately in a very large number of cases.—R. G. H.

Use and abuse of the THYROID. Means (J. H.), Boston M. & S. J., 1922, 187, 164-168.

The author takes up the discussion of the value of thyroid extract in diseases of the thyroid gland. He then warns against its use in the treatment of obesity. Three metabolism charts are shown.—J. C. D.

The effects of THYRO-PARATHYROIDECTOMY on the guinea-pig
Sur les effets de la thyro-parathyroïdectomie chez le cobaye. de Mira (F.), *J. de Physiol. et de path. gén. (Par.)*, 1919, 17, 976-980.

From the results of the operation of thyro-parathyroidectomy on 12 guinea-pigs, de Mira concludes that the total extirpation of this apparatus is fatal for these animals. The animals died in from 2 to 57 days. They exhibited apathy. There were general muscular fibrillations. Attacks of tetany preceded death. The animals operated upon lost weight. The author concludes that age is not a factor in the resistance to the loss of the glands.—F. S. H.

The effects of THYROID, THYROXIN and other iodine compounds upon the acetonitrile tests. Miura (M.), *J. Lab. & Clin. M. (St. Louis)*, 1922, 7, 349-356.

A reinvestigation of the activity of iodine in different samples of thyroid and in the other iodine compounds, including thyroxin, with the acetonitrile test. The studies showed that when desiccated thyroid is fed to mice it protects them against poisoning with acetonitrile. The thyroid seems to be efficient in proportion to the amount of iodine contained. Potassium iodide and di-iodotyrosine gave no protection against acetonitrile in whatever quantity fed. When thyroxin was fed in such an amount that it furnished one-third the iodine provided by the most active thyroid fed, a greater protection was given in some cases. Increasing the amount of thyroxin decreased the protection against acetonitrile and caused loss of weight of the animals.—F. S. H.

(THYROID) Endemic goiter in the Republic of Mexico (Contribución al estudio del bocio endémico en la República Mexicana). Nájera (F. C.), *Rev. Mex. de biol.*, 1920, 1, 47-60.

This is a very good, though brief, description of the distribution of goiter in Mexico. There is also a discussion of the probable causes of appearance of endemic goiter in the regions in which it is found, based on similar observations in other countries by other workers. The methods for prophylaxis advocated are those already known.—F. S. H.

(THYROID) Goiter prophylaxis (Zur Kropfprophylaxe). Oswald (A.), *Schweiz. med. Wchnschr. (Basel)*, 1922, 52, 313-315.

Oswald criticises the size of the dose used by Marine and Kimball as being too large. The claim is made that 8 mg. of iodine daily and even 2 mg. daily is sufficient as a prophylactic measure and avoids the danger of iodism.—F. S. H.

(THYROID) Case of paroxysmal hemoglobinuria benefited by ENDOCRINE treatment (Un cas d'hémoglobinurie paroxystique corrigée par l'opothérapie endocrinienne). Pareja (J. M.), *An. Fac. de Med. (Montevideo, Uruguay)*, 1921, 6, 209-228.

A man of 27 began to excrete blood in the urine when 15 years old after exposure to extreme cold. His brother had the same affliction. The patient showed a normal cardio-vascular system. The apex of the right lung was slightly obscure. The external genitals were hypoplastic as was the prostate. Distribution of pubic hair was feminine. Ossification of the epiphyses was apparently normal. When 1 mg. of adrenin was injected no tachycardia, polyuria or glucosuria was produced. Phystostigmine slowed the pulse for only a few minutes. Atropine failed to modify the rate of the heart or affect the pupil. Thyroid opotherapy caused an increase in nitrogen excretion. The thyroid was not clearly palpable. The sella turcica was normal. Mentality was sub-normal for the age. Libido was absent. The diagnosis of hypothyroidism was made. The blood picture was about normal. With the exception of the hemoglobin, the urine was normal. During the attacks of hemoglobinuria characteristic changes in blood and urine occurred. An eosinophilia appeared. A positive Wassermann was given. Specific treatment for the latter apparently had but little effect on the hemoglobinuria. However, when thyroid gland substance, beginning with 25 mg. and increasing to tolerance, was given, improvement was marked.

—F. S. H.

Cicatrization of the wound in THYROIDECTOMIZED guinea-pigs (Sur la cicatrization des plaies chez les cobayes éthyroïdes). Parhon (C. J.) & Savini (E.), *Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy*, 1919, 1, 4-5.

Cicatrization in thyroidectomized guinea-pigs is delayed more than in test animals which have been similarly wounded but not thyroidectomized.—F. S. H.

Changes in the **THYROID** in a case of manic-depressive psychosis with a predominance of the phenomena of confused melancholia (*Altérations importantes de la glande thyroïde dans un cas de psychose maniaque-dépressive avec prédominance des phénomènes de mélancolie confuse*). Parhon (C. J.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 33-37.

The follicles in the gland removed from this case at autopsy were small and contained but little if any colloid. Vascularization of the gland was extensive.—F. S. H.

Case of migraine cured by **THYROID** treatment (*Sur un cas de migraine guéri par le traitement thyroïdien*). Parhon (C. J.) & Hortolomei (N.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1919, 1, 68-70.

The administration of 0.025 grams of thyroid substance every other day produced an improvement in the disorder mentioned in the title.—F. S. H.

Anatomical and pathological studies of the **THYROID** in the affective psychoses (*Récherches anatomo-pathologiques sur la glande thyroïde dans les psychoses affectives*). Parhon (C. J.) & Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1920, 2, 15-42.

A total of 9 cases is described in some detail. The general results of the observations indicate to the authors that the thyroid is frequently modified in the affective psychoses.—F. S. H.

Anatomical and pathological studies of the **THYROID** in chronic deliria (*Récherches anatomo-pathologiques sur la glande thyroïde dans les délires chroniques*). Parhon (C. J.), & Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1920, 2, 49-56.

Histological studies of the thyroids from 6 insane patients. All of the glands showed abnormal cell pictures.—F. S. H.

Histological studies of the **THYROID** in the insane (*Observations histopathologiques sur la thyroïde chez les aliénés*). Parhon (C. J.) & Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 104-111.

A series of cursory observations.—F. S. H.

The relative frequency of lipid granulations in the cells of the **THYROID** in different pathological conditions (*Sur la fréquence relative des granulations lipoides dans les cellules thyroïdiennes*

dans différents cas pathologiques). Parhon (C. J.) & Stocker (Alice), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 154-155.

The authors found constant increase of lipid granules in the thyroid in senile dementia.—F. S. H.

(**THYROID**) Exophthalmic goiter in pregnancy (Consideraciones sobre un caso de bocio exoftálmico y embarazo). Pasman (F. R.) & Mestre (R.), Semana méd. (Buenos Aires), 1921, 28, 435-437.

A case of exophthalmic goiter in pregnancy is described, with improvement in symptoms following delivery. The relationship between exophthalmic goiter and pregnancy is not clear. In some instances, pregnancy is favorable to the course of the disease; in others, pregnancy has no influence; while in still others, pregnancy is of distinct harm. Exophthalmic goiter is not often seen in pregnancy. Halliday found 1 case in 1500 women; Bonnaire, 1 in 1000 women; Peralta Ramos, 1 in 12,000; Pasman found it still more rare. In the Rawson Hospital a single case was seen in ten years. However, the apparent rarity of exophthalmic goiter in pregnancy may to an extent be explained by the tendency of the obstetrician to overlook the larval forms of the disease which are mistaken for hysteria, neurasthenia, and the like. At times pregnancy may be the exciting cause of exophthalmic goiter. This is probably due, first, to a deviation of the physiological hyperfunction of the ductless glands, especially the thyroid, and, second, to the toxemia of pregnancy. A larval form of the disease may occasionally be whipped up into an outspoken manifestation of the syndrome by pregnancy.

—I. B.

(**THYROID**) Goiter. Pern (S.), N. York M. J. [etc.], 1922, 115, 409-413.

According to Pern, exophthalmic goiter is only the extreme degree of thyrotoxic goiter. Goiter, with signs of hypo- or hyperthyroidism, is in each case a hypertrophy to meet some demand. This demand, a basic cause, is toxemia. The type of goiter, in turn, is markedly influenced by calcium and iodine deficiencies or excesses. Colloids depend upon calcium for their high viscosity. Iodine added to a colloidal gel beyond a certain point reduces its rigidity; sufficient will liquefy it. If sufficient iodine is added to a colloid to prevent its setting and calcium lactate is added in quantity sufficient not only to precipitate all of the iodine as calcium iodide but also to combine in the form of colloid, it will again gel. Goiter of the large type accompanied with hypothyroidism and cretinism are prevalent in limestone districts. Individuals living in such districts are literally saturated with calcium. The alleviation of this type of goiter is accomplished by the administration of iodine; hence, it would appear that myxedema results because of an accumu-

ation of colloid rich in calcium, which in the presence of iodine is rapidly absorbed owing to the antagonizing action of the iodine to the calcium and the consequent liquefaction of the colloid. In districts where the water is free from calcium, goiter is prevalent, but it is marked by symptoms of hyperthyroidism. Women of such districts are prone to severe post-partum hemorrhages and delayed coagulation time of the blood. This condition can readily be corrected by the administration of calcium lactate. Goiters of calcium free water districts are usually small, extremely vascular, free from colloid, and are associated with symptoms of hyperthyroidism and increased blood iodine. Treatment with iodine preparations increases the symptoms. It therefore appears that in the presence of infection or intoxication that the thyroid gland hypertrophies; the type of hypertrophy depends upon whether the body colloids show a preponderance of calcium or iodine.—H. W.

(THYROID) Severe Basedow's DIABETES with diabetic coma (Note sur un cas de diabète grave basedowien avec coma diabétique). Popovici (C.) & Ionescu (A. St.), Bull. et mém. Soc. neurol., psychiat. et psychol. de Jassy, 1921, 2, 156-158.

Case of Basedow's disease which had been treated with intensive radiation. This was followed by diabetes from which the patient died. The appearance of the diabetes coincided with the regression of the goiter.—F. S. H.

(THYROID) Surgical treatment of goiter. Quay (J. E.), Texas State J. M. (Ft. Worth), 1922, 18, 208.

A summary of the classifications and treatment of toxic thyroids, as practiced at the Mayo Clinic.—C. R.

(THYROID) Substernal goiter, with pressure symptoms. Ratchford (B. K.), Tr. Ass. Am. Physicians (Phila.), 1920, 35, 258-262.

See Endocrinology, 1921, 5, 521.

(THYROID) The frequency of Basedow's disease in Vivarias (Fréquence du syndrome de Basedow dans le Vivarias). Regnault (F.), Bull. Acad. de méd. (Par.), 1921, 3, s. 85, 193-195.

Regnault comments on the relative frequency of occurrence of the Basedow syndrome in Vivarias (a province south of Lyons, France). Females already possessing a simple goiter constitute the majority of patients. Goiter is still endemic in that region, though to a lesser extent than was the case 20 years ago. The Basedowian syndrome follows one or more pregnancies or an emotional strain. A number of instances resulted from the recent war conditions. The chief manifestations are an increased force of the heart impulse with tachycardia, tremor, a changed expression, and a brilliancy of the eyes, but there is no exophthalmos. There is also diminished capac-

ity for work, insomnia, restlessness, and irritability. Metrorrhagia is common. The development of toxic symptoms in these persons seems to be instigated by their excitable, impulsive temperament.

—I. B.

HYPERTHYROIDISM in pregnancy. Robinson (A. L.), J. Obst. & Gynæc. Brit. Emp. (Lond.), 1922, 29, 296-302.

A report of 15 cases of hyperthyroidism in pregnant women. The clinical picture, in general, is one of mild or atypical Graves' disease. These patients were originally treated as neurotic women made worse by the strain of pregnancy, but they obtained little improvement from bromides, iron, aperients, etc. Later, the association of prolonged lactation and deficient nutrition suggested calcium depletion as an important etiological factor, while certain of the clinical features (e. g., muscle cramps and increased nervous excitability) had a clear resemblance to tetany, which is itself a manifestation of parathyroid disease, and a common condition of pregnancy in some countries. On these grounds the author has employed parathyroid and calcium lactate in all cases, usually 1-10 gr. of the former and 20 gr. of the latter each night. He has permitted lactation in those patients who have not been seriously affected, and continued the treatment with calcium lactate, omitting the parathyroid. In the severer types he has forbidden lactation and given calcium and pituitary extract. The results are described as encouraging.—E. N.

(THYROID) Goiter summary. Rosser (C. M.), Texas State J. M. (Ft. Worth), 1922, 18, 196.

The writer believes that surgery in uncomplicated colloid goiter is unwise except for relief of pressure or deformity, but advises early removal of all adenomatous goiters, which he says are potentially toxic. Hyperplastic goiter should always be operated upon and the use of the x-ray and radium should be regarded as an adjunct only to operative removal. He believes that it is unnecessary to deceive the patient concerning the operation, and that local anesthesia in the hands of a surgeon of sufficient tact and patience offers the ideal method.—Author's Abst.

(THYROID) Treatment of MYXEDEMA (Traitement du myxœdème). Sainton (P.), Progrès méd. (Par.), 1920, 35, 409.

A discussion of thyroid opotherapy and adjuvant measures of treatment. Oral ingestion of thyroid extract is advocated as against injection methods of administration. In myxedema of syphilitic origin arsenicals are of course indicated. In children calcium preparations are at times of benefit. Opotherapeutic treatment is increasingly beneficial as the age at which the disorder appears is advanced.

—F. S. H.

(**THYROID**) Respiration in Graves' disease (*La respiration des Basedowiens. Étudiée à l'aide des méthodes actuelles: masque de Pech, spirométrie, radioscopie, etc.*). Sainton (P.) & Schulmann (E.), *Ann. de méd. (Par.)*, 1922, **12**, 174-188.

Studies of the respiratory rate and rhythm in patients with Basedow's disease. The results indicate that the polypnea, inferior thoracic expansion, diminished diaphragm incursion, lowered limit of voluntary apnea, and diminution of the respiratory capacity are the consequence of the disorder and not the result of a concomitant rhino-pharyngeal or pulmonary lesion. The oculo-respiratory reflex is positive.—F. S. H.

(**THYROID**) Hereditary and familial goiter and cervical sympathetic nerve paralysis (*Gozzo e paralisi del simpatico cervicale ereditari e familiari*). Samaja (N.), *Riv. di patol. nerv. (Firenze)*, 1920, **25**, 284-297.

Three brothers were affected by goiter. One of these having unilateral anhidrosis married a woman with goiter and sympathetic lesions. From this marriage six children were born, four having goiter and sympathetic lesions, and one, a daughter, having myxedema and hypophyseal dystrophy; a nephew also had thyroid hypertrophy. Another of the three brothers had a healthy wife, but he had two sons with goiter and a third with manifest goiter, but with sympathetic involvement. The nephews, sons of the first of the brothers, all had large thyroids; the second daughter was unmarried; the third, who is epileptic with anhidrosis on the right side, had two sons with this hereditary goiter, and one of these with typical Bernard-Horner disease. Thus there were three generations with goiter; and at least two, and perhaps three, with sympathetic disorders. According to the author, this combination has not previously been reported.—P. M. N.

Proteinogenous amines in the **THYROID** (*Über das vermutliche Vorkommen von proteinogenen Aminen in der Schilddrüse*). Sammartino (U.), *Biochem. Ztschr. (Berl.)*, 1922, **131**, 219-225.

An exhaustive attempt to obtain proteinogenous amines from fresh thyroid tissue failed to give any evidence that such compounds occur there naturally.—F. S. H.

The glucose mobilization rate in **HYPERTHYROIDISM**. Sanger (B. J.) & Hun (E. G.), *Arch. Int. Med. (Chicago)*, 1922, **30**, 397-406.

Ten normal controls and ten well marked cases of exophthalmic goiter were studied under identical conditions. Carbohydrate utilization was computed from studies of the blood sugar, the respiratory quotient and the total metabolism, before and after glucose injection. The blood sugar curves in the control cases were entirely normal, while those in the cases of hyperthyroidism, for the most

part, showed the usual variation—an abnormally high peak maintained over a prolonged period. The respiratory quotients in the normal cases revealed normal carbohydrate storage and response, while those in the cases of hyperthyroidism showed a greater and more rapid rise, which made for a striking increase in the carbohydrate utilization. In cases of hyperthyroidism there is a deficiency in the ability to store carbohydrate. This makes for a carbohydrate plethora and this stimulates carbohydrate metabolism. This inability to store glucose is probably a failure of liver storage, due to some toxic change in the liver caused by the disease.—H. L.

(THYROID) Increase of goiters (Zunahme der Strumen). Schick, Wien. klin. Wchnschr., 1922, 35, 663.

A short note. In Vienna the number of goiters has been recently increasing. Klinger's idea of compelling the school children to take very small quantities of iodine is an excellent preventative measure and is recommended also in Vienna.—J. K.

Hyperplasia and hypersecretion of the THYROID in children (Hyperplasie und Hypersekretion der Schilddrüse bei Kindern und Jugendlichen). Schlesinger (E.), Ztschr. f. Kindhk. (Berl.), 1920, 27, 207-230.

In regions of endemic goiter the author finds that new born infants often show a transient hyperplasia of the thyroid. This subsides in a few months. A second wave of thyroid enlargement appears in girls at 6 or 7 and in boys at 9, reaching its height before or during puberty. The thyroid enlargement is usually due to hyperplasia rather than to a nodular growth. About one-sixth of the boys and one-third or more of the girls show cardiovascular disturbances, though severe intoxication is rare. The children with this mild hyperthyroidism usually show a mental and physical development in advance of their years. The sexual development in the girls is likewise advanced.—C. H. G.

(THYROID) Pathology of goiter. Scott (A. C.), Texas State J. M. (Ft. Worth), 1922, 18, 200.

Scott calls attention to the fact that there is no distinguishable pathological difference between toxic and non-toxic adenomas of the thyroid, and that there are no pathological findings in toxic adenomas indicative or corresponding to toxicity, while there are distinct differences in the pathology, symptomatology and physical findings as between cases of toxic adenoma and exophthalmic goiter.

—C. R.

(THYROID) Changes in the muscles in myxedema and myotonia atrophica (Beiträge zur Kenntniss der Muskelveränderung bei Myxodem und Myotonia atrophica). Slauck (A.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.), 1921, 67, 276.

Heidenhain has described certain changes of fibrous nature in the muscles in myotonic dystrophy which are analogous to those found in the musculature of congenital myxedema. The electrical excitability of the muscles from each disorder is also similar. In myxedema there is a high grade lowering of the irritability, the same is true of myotonia. On account of these similarities the "Kuprevidin" treatment of myotonia is indicated.—F. S. H.

(THYROID) Special disorders of the heart from goiter. Sloan (E. P.), Illinois M. J. (Chicago), 1918, 33, 152.

Pressure symptoms with circulatory disturbances from pressure on the blood vessels in the neck were present in 30% of the operative goiter cases. Other disturbances that were observed as traceable to the goiter were: endocarditis, premature contractions, auricular flutter, auricular fibrillation and myocarditis. Removal of the goiter benefits or cures these conditions when it has caused them. Heart-block and defects in transmission of impulse are not caused by goiter and are not benefited by removal of goiter that may be present.
—F. S. H.

(THYROID) Some ways of using the electric current in exophthalmic goiter. Solis-Cohen (S.), Am. J. Electrotherap. & Radiol. (N. Y.), 1921, 39, 59-66.

The pathogenesis, clinical aspects and a few measures in electrotherapy of exophthalmic goiter are briefly discussed. Since all cases of Graves' disease differ, no two patients can be treated alike; moreover, in no patient will a given therapeutic measure produce good results from beginning to end. There are two types of patients with exophthalmic goiter: first, those highly toxic, with marked thyroid activity, occasional fever, marked cardiac and nervous excitement and very high blood pressure; second, the milder type which is more sluggish in its evolution. Between these two extremes are the various gradations commonly met with. In treatment, rest is the first requisite, followed later by electricity. Autocondensation is a useful adjunct in management of high blood pressure; 200 to 300 milliamperes are administered for 20 minutes daily, or less often according to circumstances. In the milder cases, the static spark or the effluve from the resonator is applied over the gland or alternately first on the one side, then on the other, of the seventh cervical vertebra when the enlargement is bilateral, or over the one side when the enlargement is unilateral. The application may be made both to the gland and over the vertebra by the use of a metal ball on a grounded strand. The strength of the current depends upon the subjective reaction, stopping short of great discomfort, and the skin over sites of application must present an erythematous reaction. The spark gap between the Leiden jars should be from one-quarter to two inches as desired, with an electrode of wood or brass placed either in contact with or at some dis-

tance from the skin over the gland, depending upon subjective and objective results. Galvanism, 5 to 10 milliamperes modified by the sinusoidal apparatus (60 to 90 interruptions per minute) placed over the side of the seventh cervical vertebra for 3 to 20 minutes, according to indications, is useful. Faradism may be combined with galvanism in the sinusoidal apparatus. The sinusoidal treatments may be first given in recent cases, the static in cases of longer duration. The old fashioned, simple galvanism is also useful, with the anode over the cervical sympathetic or the vagus, sometimes over the thyroid, the cathode over the sternum. In sluggish cases iodine ionization may be given; the cathode being placed over a pad moistened with a solution of potassium iodide or sodium iodide. Iodine ionization, however, should be employed only in cases in which the element of hyperthyroidism in the Graves' syndrome is absent, and the nervous symptoms are mild. The treatment of exophthalmic goiter may become surgical only when diagnosis is belated, in which instances there may be extreme pressure symptoms or a very great degree of hyperthyroidism. Even under such conditions in patients skillfully operated upon the essential autonomic and general endocrine disorder still persists, requiring appropriate nonsurgical management. In exophthalmic goiter treatment is nonsurgical in 90% to 95% of cases. Individualization is the keynote in treatment. In this protracted illness no case should be undertaken for treatment unless the patient consents to remain under observation for at least six months.—I. B.

(THYROID) Goiter. Stanton (J.), Boston M. & S. J., 1921, 184, 693-696.

Brief general review.—H. W.

(THYROID) Experimental studies of the hypothetical relation between Basedow's disease and tuberculosis (*Récherches expérimentales sur les relations hypothétiques entre la maladie de Basedow et la tuberculose*). Steck (H.), Schweiz. med. Wchnschr. (Basel), 1921, 51, 535-538.

Although there may occur a gross similarity in symptomatology of the two diseases under investigation Steck fails to find experimental evidence of a common etiology. By the administration of graduated doses of adrenin, plus the blood plasma from patients with Basedow's disease and from others with tuberculosis, to eviscerated guinea-pigs deprived of the central nervous system an analysis was made possible which demonstrated that in the majority of cases of the former disease there could be found evidence of the presence in the blood of substances of thyroid origin, while the tubercular cases furnished no such evidence. The blood from the patients with Basedow's disease augmented the constriction of the blood vessels obtained with adrenin. The blood of the tuberculous patients had no reenforcing action.—F. S. H.

(**THYROID**) Technic of goiter operation (Zur technik der Strumektomie). Streiszler, Wien. klin. Wchnchr., 1922, 35, 664.

The author recommends that both lobes be removed and that the operation be started at the isthmus. No ligation of the large vessels is made.—J. K.

Radium emanations in exophthalmic goiter. Blood vessels of adenomas of **THYROID**. Terry (W. D.), J. Am. M. Ass. (Chicago), 1922, 79, 1-3.

Including a former report, Terry brings his series of cases treated by radium emanation up to 33. Only patients with an extreme degree of hyperthyroidism were included; and this method of treatment was used only with the idea of converting them into better risks for major surgical procedures. Capillary tubes containing radium emanation were inserted into the substance of the thyroid gland, using local anesthesia. The ensuing pathologic changes are described. Final results are reported in 16 cases. Two were cured by radium emanation therapy alone; 10 were cured after resection; 4 died from two days to nine months after resection, 2 of them from hyperthyroidism. Experimental work on the anatomy of the blood vessels of thyroid adenomas is also reported in brief. The frequency of hemorrhage in adenomas is attributed to the weak walls of the intracapsular veins.—W. M. A.

(**THYROID**) The influence of **THYROXIN** on alcoholic fermentation (Ueber den Einfluss des Thyroxins auf die alkoholische Gärung). Tomita (M.), Biochem. Ztschr. (Berl.), 1922, 131, 174-177.

The addition of thyroxin to mixtures of yeast and glucose resulted in an acceleration of the fermentative processes.—F. S. H.

Hen-feathering induced in the male fowl by feeding **THYROID**. Torrey (H. B.) & Horning (B.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 275-279.

The results of the experiments as given in the title did not occur in castrated males and hence it appears that the appearance of hen-feathering in normal males when fed thyroid is dependent on the presence of luteal cells.—F. S. H.

Two cases of acute suppurative **THYROIDITIS** (Deux cas de thyroïdite aiguë suppurée). Tourneux (J. P.), Progrès méd. (Par.), 1920, 35, 371-372.

Cases are cited in which the inflammation is induced in glands primarily healthy and not complicated by goitrous degeneration. In the first case Eberth's bacillus was isolated in pure culture; in the second, pneumococcus and streptococcus were found.—F. S. H.

(**THYROID**) Mongolian idiocy in a Chinese boy. Tumpeer (I. H.), J. Am. M. Ass. (Chicago), 1922, 79, 14-16.

This case, presented in detail and illustrated, is stated by Tumpeo to be the first reported occurring in any but the Caucasian race. The findings are typical, including the recently noted changes in the sella turcica. The basal metabolic rate was within normal limits.

—W. M. A.

The rôle of heredity in THYROID pathology. Vallery-Rodot (P.), *Lancet* (Lond.), 1922, i, 24-26.

A discussion of heredity in disorders of the thyroid gland together with the presentation of several cases. There is very frequently a strong hereditary or a familial tendency to abnormal thyroid function. These tendencies are described as being "similar" or "dissimilar," that is the child may inherit a tendency to Basedow's disease when the mother has it or he may have myxedema. Several members of a family are said to be affected frequently, some inheriting one type of disorder and others another type. There is often dysfunction of other endocrine glands in cases showing strong evidence of the congenital and familial factors. The author believes that the hereditary tendency to thyroid abnormality makes the gland more susceptible to attacks from syphilis, infectious diseases, intoxications, etc. He believes also that efforts at prophylaxis might be of great value if the hereditary element were worked out and the mother treated during pregnancy and lactation.—I. M.

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ABSENCE OF THE PROSTATE ASSOCIATED WITH ENDOCRINE DISEASE, NOTABLY HYPOPITUITARISM; WITH HISTORIES OF EIGHTEEN CASES*

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STATUS OF THE PROSTATE AS A GLAND OF INTERNAL SECRETION

It is still a question whether or not the prostate deserves to be classified among the glands of internal secretion. If it be one of them, it certainly has very little importance as compared with the thyroid, the pituitary gland, the ovaries, the testicles, the adrenal, the thymus and the pineal body. For the present we may perhaps place it in the doubtful group composed of the mammary glands, the placenta and the carotid gland.

In 1907, Wallace (1) considered it proved that the prostate must be regarded a sexual gland for the following reasons: it is confined to the male sex; it enlarges rapidly at puberty, simultaneously with the other sexual organs; it exhibits seasonal activity in animals such as the mole and hedgehog which only pair at certain times of the year; it fails to grow in eunuchs, that is, individuals that are castrated in youth; and it atrophies after castration in adults. The above facts nevertheless do not

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prove that the prostate elaborates an internal secretion in the sense that the thyroid and pituitary do.

Certain investigations suggest, however, that it has such a secretion. Thus, DuBois and Boulet (2) in 1919 demonstrated that intravenous injections of extracts of normal prostate cause a contraction of the bladder, whereas, hypertrophied human prostate had no such effect. These findings led the authors to conclude that there is an internal secretion of the prostate which acts as an excitant of the bladder muscle.

Bogoslovsky and Korentchevsky (3) made observations on the metabolism of two normal and six castrated dogs that were given intravenous injections of emulsion of prostate or of testicle or both. Normal dogs showed a slight increase of nitrogen exchange and diuresis under the influence of injections of prostate. In castrated dogs this phenomenon was more marked, there being an increase amounting to from 8 to 10 per cent. The simultaneous injection of prostate and testicle caused an increase of nitrogen up to 17 per cent and of diuresis up to 25 per cent. They conclude that the prostate constitutes a powerful stimulant to the internal secretion of the testicle, and that the internal secretion of the testicle exercises a stimulating influence on the exchange of protein substances especially.

Macht and Matsumoto in 1920 (4) performed experiments to determine whether prostatic extracts *in vitro* have any specific action on isolated genito-urinary organs. They concluded that no specific action exists. Macht (5) reported in 1921 that feeding prostate hastens the metamorphosis of frog and salamander larvae, but that, unlike thyroid, it causes no shrinkage of the animals. He again found that extracts of prostate had no particular influence on the contraction of smooth muscle such as the bladder. He also pointed out that prostatic extract hastened coagulation of the blood, but that this is due to kephalin and not to a specific substance.

On the clinical side, Kondoleon (6) noted striking enlargement of the mammae following prostatectomy in two men over seventy years of age. He jumped to the conclusion that the internal secretion of the prostate prevents enlargement of the mammae in men. Zuckerkandl (7) immediately took issue with this report and criticised the author for not describing the histological process in the enlarged breasts; and furthermore, he

called attention to the fact that what surgeons call prostatectomy is only the removal of the hypertrophied submucous glands, while the prostate itself remains in the body. While the above observations do not include all the work done on a possible internal secretion of the prostate, the results are sufficiently meager to forbid any assumption at this time that the prostate is an in-cretory gland.

INFLUENCE OF THE TESTICLE ON THE PROSTATE

Castration was one of the earliest of surgical procedures, and in 1775 John Hunter called attention to the fact that castration carried out in youth or infancy causes hypoplasia or want of development of the prostate. About a century later Griffiths, White and Guyon (1) added the interesting fact that castration in adult life causes atrophy of the prostate. Griffiths, for instance, in 1889 reported that the prostate of an adult dog a year after castration was to all purposes as atrophied as if the dog had been castrated in youth. The rate of this atrophy was very rapid, being very pronounced three weeks following operation. This experiment was confirmed by White in 1893 (1), Guyon in 1895 (1), and Wallace in 1906 (1). These experiments prompted White to propose castration as a cure for hypertrophied prostates.

In 1893, Griffiths (8) enlarged our knowledge in respect to gonad insufficiency, at the same time introducing the term "eunuchoid" to describe a type of individual who was lacking in testicular secretion but had not been castrated. He reported two cases of men aged 30 and 21 respectively who were of peculiar form, with narrow shoulders, broad pelvis, round and plump neck, beardless face, high pitched voices, large breasts, and whose genitalia were infantile. In one patient, practically no prostate was palpable per rectum; that is to say, a thickening was felt, but no definite gland. The other was examined post mortem and the prostate was hardly more than one-third its natural size. Microscopic glandular tubules could be detected in the prostate, but they were comparatively few.

In 1916, Morris (9) added an interesting point by recording the case of a man aged 27 who lost both testicles at thirteen years from mumps. The scrotum was shriveled and apparently empty, penis small, skin wrinkled, hair sparse; the prostate gland

could not be felt. A human testicle was grafted, part into the abdominal rectus muscle and part into the scrotum. Considerable improvement followed as shown by erections and growth of the penis. He noted that apparently a little line of prostatic tissue could be made out at the site of the prostate gland. The above reports and many others substantiate beyond question the profound influence exercised by the internal secretion of the testicles upon the development of the prostate.

THE INFLUENCE OF THE PINEAL AND SUPRARENAL GLANDS UPON THE PROSTATE

Some rather bizarre syndromes are on record which show striking relationships between the pineal gland and the genital apparatus, and similarly between the suprarenal gland and sexual development. These syndromes for the most part result in an amazing sexual precocity, and we might expect in such cases to find the prostate enlarged. I cannot find any direct reference to the prostate in diseases of these glands, but possibly such an observation has been recorded. Unfortunately, I have not yet seen one of these peculiar endocrine disturbances, so that I do not know the condition of the prostate in such cases.

Hoskins in 1916 (10) made some valuable experiments on the feeding of suprarenal tissue to young white rats. He noted that the ovaries and testicles were very definitely hypertrophied, but that the other ductless glands were not affected. Unfortunately, he does not mention the prostate. It would have been interesting to know whether prostate enlargement occurred also.

THE INFLUENCE OF THE PITUITARY UPON THE GENITALIA AND THE SECONDARY SEX CHARACTERS

Clinical hyperpituitarism produces gigantism before adolescence and acromegaly after puberty. In the earlier stages of acromegaly we are acquainted with examples of excessive sexual libido, and in gigantism with instances of premature acquisition of sex power and secondary sex characters. Most of these patients, however, come to the physician in the late stages of the disease when pituitary inactivity has supervened, and then we find, in the female, characteristic obesity, amenorrhoea and sterility; and in the male, diminished libido and potentia; and in both a high degree of atrophy of the sex glands. This well recognized relationship between the pituitary and the sex ap-

paratus is exemplified even more emphatically in primary hypopituitarism. The Froehlich (11) syndrome, described first in 1901, consists of skeletal undergrowth, obesity, and sex infantilism; the Lorain (12) type likewise demonstrates skeletal undergrowth and sexual aplasia, but *without* adiposity; the Neurath-Cushing (13) variety of dyspituitarism consists of skeletal *overgrowth* with obesity and sexual infantilism; the feature common to all in these clinical disturbances is sexual infantilism.

Attempts have been made to produce hyperpituitarism experimentally. Those who chose transplantation of pituitary tissue as a method of producing hyperpituitarism failed in their efforts. Several workers, however, pursued a more fruitful method. Goetsch (14) fed anterior lobe pituitary, posterior lobe pituitary and whole gland pituitary to young rats and obtained very positive results. He noted that when whole gland was fed to young rats in excessive doses these animals failed to gain in weight, lost appetite, suffered from diarrhoea and certain nervous manifestations. He found that this was due to the posterior lobe element. The posterior lobe alone did not stimulate growth in general or the development of the sex glands; whereas the feeding of anterior lobe extract caused more vigorous body growth than occurred in the control animals, and it brought about an earlier and more active genital development. In his report he specifically mentioned the effect of anterior lobe feeding on the prostate gland, which showed, like the sex glands, an earlier development and activity. (This work has not been confirmed). Conversely many authors [notably Crowe, Cushing and Homans (15, 16), Blair Bell (17), and Aschner (18)] proved by producing hypopituitarism experimentally, that the genital apparatus is markedly retarded in its development and that this hypoplasia included the prostate as well as the testes, penis and vas deferens.

THE PROSTATE IN CLINICAL HYPOPITUITARISM

In view of the striking genital abnormalities repeatedly emphasized in clinical hypopituitarism, and in view of the specific mention of undeveloped prostates in experimental hypopituitarism, it seems rather surprising that no reference to the prostate has been made in the innumerable case reports of Froehlich.

Lorain and Neurath-Cushing hypopituitarism. Accordingly, in 1920, I (19) placed on record five cases of preadolescent hypopituitarism, in three of which no prostate could be felt by rectal examination, and in two of which only a very diminutive organ could be recognized. Eighteen cases will be reported in this paper. Apparently it is not customary for pediatricians to examine the prostate in their routine physical examinations, probably because disease of this organ in childhood rarely if ever occurs. Certainly, none of the standard books on diseases of infancy and childhood that I have consulted make any mention of the prostate gland. Rectal examinations, however, are frequently made in children for various reasons, and perhaps it might be well in future to note the size of the prostate, especially in boys showing other evidences of sex infantilism.

Since some may have the impression that the prostate in childhood is so small as to be difficult to palpate, it may be well to include herewith a brief description of its size from birth to puberty. Lowsley (20) in 1912 reported his studies on the development of the human prostate. He states that the gland begins to develop at the third month of fetal life. The tubules which compose it make their first appearance as solid epithelial outgrowths from five distinct parts of the prostatic urethra. The first appearance of muscular fibers developing around the tubules is found at the sixteenth week. At birth the organ is very small, and it continues comparatively so until the time of puberty. According to the researches of Gross (21) of Louisville, it weighs only thirteen grains at the time of birth; his report on the size, form and weight of the prostate, from that period up to adult age, is very complete and may be given here.

“The Prostate at Birth. Width at base, 4 lines; a little above middle, 5 lines; at apex, 2 lines; length along the middle, 4 lines; at the edge, $4\frac{3}{4}$; thickness at base, 2 lines; at middle, $3\frac{1}{4}$; and at apex, $1\frac{1}{4}$. Weight, 13 grains. (A “line” is an obsolete unit of measurement equivalent to one-twelfth of an inch.)

“The Prostate at 4 Years. Breadth at base, 6 lines; just above the middle, 7; and at the apex, $2\frac{1}{2}$; length along the middle, 6 lines; and 7 lines at the margin; thickness at base, $2\frac{3}{4}$ lines; at the middle, 4; and at apex, 2. Weight, 23 grains.

“The Prostate at 12 Years. Width, $8\frac{1}{2}$ lines at base; $9\frac{1}{2}$ above the middle, and 3 at apex; length along the middle, 8 lines.

and $8\frac{1}{2}$ at the edge; thickness at base, 3; middle, $4\frac{1}{2}$; and at apex, $2\frac{3}{4}$. Weight, 43 grains.

"The Prostate at 14 Years. Width at base, 11 lines; at middle, $9\frac{1}{2}$; at apex, 4; length along the middle, 8 lines, and 10 at margin; thickness, $3\frac{1}{2}$ at base, 5 at middle, and 3 at apex. Weight, 58 grains.

"The Prostate at 20 Years. Breadth at base, 14 lines; at middle, 16; at apex, $5\frac{1}{2}$; length along middle, 15 lines, and at edge, 16; thickness at base, 8 lines; middle, 10; and apex, $5\frac{1}{4}$. Weight, 4 drachms and 1 scruple."

Mr. H. Bell, in an inaugural thesis which he published in Paris, made observations, which have been copied by Malgaigne in his *"Traite d'Anatomie Chirurgicale,"* resulting from dissection of upwards of forty subjects ranging between two and fifteen years of age. They are as follows:

Ages	Diameter Transverse mm.	Posterior Oblique Diameter mm.	Transverse Posterior Diameter mm.	Transverse Anterior Diameter mm.
2 to 4 years.....	12.40 to 13.5	4.5 to 5	2.25	1
5 to 10 years.....	13.5 to 17	5 to 7	4.5 to 5.6	1
10 to 12 years.....	16 to 19	6 to 8	4.5 to 5.6	2.25 to 3.4
12 to 15 years.....	19 to 22	8	4.5 to 5.6	3.4

Sir Henry Thompson dissected one specimen at twelve years, which forms a preparation at the College of Surgeons, and the weight coincides very closely with that of one at the same age in Gross' series.

At twelve years: weight 40 grains.
Length—1 inch.
Breadth— $\frac{3}{4}$ inch.
Thickness— $\frac{3}{8}$ inch.

We must not overlook the researches of Deschamps made on a great number of bodies. In his *"Traite Historique et Dogmatique de la Taille,"* he reports as follows: 1. "In subjects from three to eight years of age, the anterior thickness of the prostate" (anterior to the urethra) "is a line and three-quarters; its posterior part two lines and a half; and its lateral parts three and a half lines;" . . . 2. "In subjects from eight to sixteen years the thickness of the anterior part is about two lines; of the posterior part, three lines; of the lateral parts, four to five lines."

Thompson states that the following general considerations are those of importance in reference to this subject.

"The position of the prostate in children differs from that in the adult subject. It is more vertically placed in the pelvis than in that of the latter. The bladder has a corresponding position, the lower fundus is less depressed, less sessile on the rectum (so to speak) than it becomes later in life. The peritoneum comes very near to the base; but as the fundus is developed in later life, the peritoneum becomes further removed, and a well marked space, or portion of the bladder (carefully noted both by the anatomist and the surgeon), remains uncovered by it beyond the prostate.

"The form of the gland is more rounded in childhood, and has less of the distinctive characters and outlines which mark the adult organ and its lobes.

"Its consistence is soft, the capsule is easily torn, the glandular structures are simple, and slightly developed, being apparently little more than simple follicles, tubular and cyst-like and ducts."

REPORT OF EIGHT CASES OF PREADOLESCENT HYPO- PITUITARISM OF THE LEVI-LORAIN TYPE OF INFANTILISM

(Prostate absent in six and very small in two)

CASE No. 1 (See Figure 1). U. C. O. P. D. No. 78887, H. Z., aged 9½ years. *Preadolescent Hypopituitarism (Levi-Lorain Infantilism) with Absence of Prostate.*

COMPLAINT: Lack of development.

FAMILY HISTORY: Negative.

HISTORY: Lived in Peru at an altitude of 14,000 feet from 14-32 months of age, remainder of life in Berkeley, California. Had measles at 7, pneumonia at 5, mumps at 5 (one side), chicken pox, acute intestinal trouble (mucous colitis?) at 3—worms removed. Tonsils and adenoids were removed at 7.

PRESENT ILLNESS: Birth weight 7 pounds, but mother says he looked very small and emaciated. At 11 months weighed 9 pounds. *Always has been extremely small for his age*, although he had very good care, hygiene and nourishment. Walked alone at 18 months; spoke individual words at 16 months and sentences at 3 years after an operation to loosen his tied tongue. Always has been very energetic and nervous. Craves water and sweets. Has enuresis occasionally even now; also great frequency of urination during the day, and nocturia twice.

EXAMINATION: Height with shoes 49½ inches; span equals height, upper measurement equals lower; weight, dressed, 52½ pounds. Hair is very dry, thick and coarse. He has external strabismus of the left eye. The thyroid is just palpable. The heart is not enlarged, but well marked systolic murmur is everywhere audible even in axilla, probably functional; *unusual bradycardia*—56 is noted. Genitalia: No pubic hair; penis perhaps a little small, redundant prepuce; *left testis in inguinal canal*; right testicle in upper part of scrotum, but outside external ring; *prostate not palpable* (Doctor L. P. Player, Urologist).

Mental Age (Binet-Simon): 9 years, no retardation.

Urine: Normal.

X-ray: *Plates of Hands*—normal for age; *Plates of Skull*—sella seems normal, but convolutional markings are rather prominent; sphenoidal angle—150 degrees.

Electrocardiogram: Unsatisfactory. Child was very restless and afraid of machine, so that heart rate was 75.

Operation November 27, 1921, by Dr. Player. *Testicles brought down into scrotal sac*.

January 6, 1922: Much less euresis since operation and greatly decreased frequency of urination.

Treatment begun with anterior lobe Pituitary (Armour), gr. 15 daily.

March 17, 1922: No more euresis.

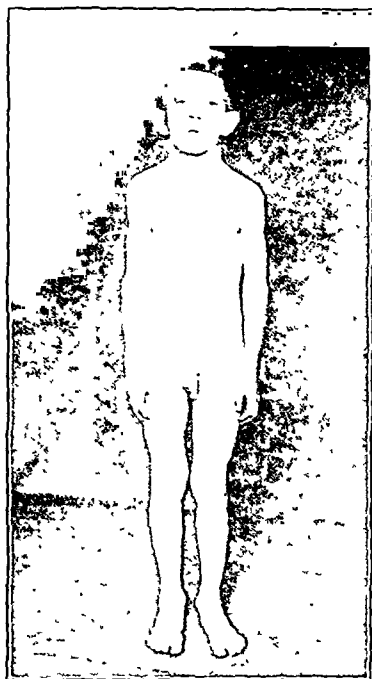


Figure 1 (Case 1). Age 10, skeletal undergrowth with sexual infantilism, undescended testicles; no prostate

CASE NO. 2 (Private case). J. B., boy, aged 14. *Hypopituitarism, Levi-Lorain type, Associated with Mental Retardation and Absence of the Prostate.*

HISTORY: Two brothers, aged 3 and 7, very well, big, strong and robust. The 7 year old brother was as large as the patient and weighed more. There are two normal sisters, aged 16 and 17. The patient was very difficult to rear. All manner of milk preparations were tried; finally successful with goat's milk. Walked when not quite two years. Did not really talk until three years of age. Measles at age of 3; whooping cough at 6; influenza at 12; scarlet fever at 13. He was a nervous child; absolutely lacking in mathematical sense; was

in the fourth grade in school. He had a good disposition; could not concentrate; played actively; no sign of puberty.

EXAMINATION: Height, 55 inches; weight, 59½ pounds; the boy is knock-kneed; he has prominent scapulae; flat feet; marked scoliosis; prominent ears; thin, narrow, funnel-shaped chest; baggy lids and heavy, expressionless eyes. Genitalia: The folds of the scrotum suggest labia majora; prominent mons veneris. The penis is normal; right testicle was only partially descended, and left testicle well up in the inguinal canal, but on stripping the canal it could be brought down so as to be palpated in the upper portion of the scrotal sac. Both testicles were atrophic and small, the right much more so than the left. *It was not possible to palpate any remnant or portion of the prostate by rectal examination.* The laboratory findings follow.

Urine: Negative.

Blood Pressure: 110/70.

Mental Age: Seven (7 years' retardation).

X-ray: Plate of Skull showed sella markedly small, both in depth and anterior posterior diameter; sphenoidal angle 152 degrees.



Figure 2 (Case 3). Age 14, sexual infantilism without adiposity; prostate not felt.

CASE No. 3 (See Figure 2). U. C. O. P. D. No. 82761, M. T. H., aged 14 years. *Preadolescent Hypopituitarism (Levi-Lorain Infantilism) with Absence of Prostate.*

HISTORY: Mother had two babies that died after birth; walked at 1½ years. Had whooping cough, measles, mumps, diphtheria; tonsillectomy and adenoidectomy. Was brought to clinic because of kleptomania and prevarication.

EXAMINATION: Span equals height and upper measurement equals lower. Height (in shoes), 60 inches; weight, dressed, 92½ pounds. Prominent frontal eminences, *broad saddle nose, rough, dry, cracked, scaly skin.* Infantile genitalia consisting of *very small penis, and small empty scrotum.* Right testis can be palpated by pushing index finger in ring and milking testis downward; appears to be about size of almond kernel. Right testis cannot be so plainly felt, though it appears to be in canal. Rectal examination: Anal sphincter of good tone; with examination there was a marked erection, penis being about two inches in length and three-quarters in diameter. Corpora

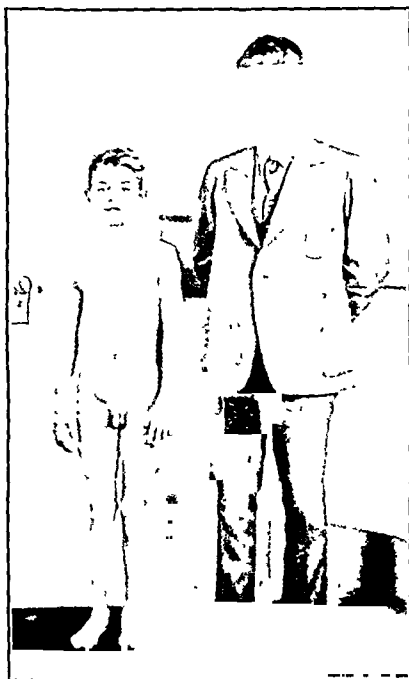


Figure 3 (Case 4). 15 years, skeletal undergrowth with sexual infantilism without adiposity; prostate very small. Normal adult in picture is 5 ft. 5 in. tall.

cavernosa could be felt along perineal floor. No "*perineal body*" felt—*entire absence of prostate.* No secretion was expressed following massage. Patient has the *external genital development of a 4 or 5 year old boy*, though there is a slight downy growth over pubic region.

V. Pirquet: Negative.

Wasserman: Negative.

X-ray Plate of Skull—large thin calvarium; skull base steep; sphenoidal angle 151 degrees. Sella small and open.

X-ray Plate of Hand—bones delicate in structure—terminal phalanges show no evidence of tufting.

Mental Age (Binet-Simon): 15 years, no retardation.

CASE No. 4 (See Figure 3). U. C. O. P. D. No. 66862, boy, aged 15 years. *Infantilism Resembling Levi-Lorain Type of Hypopituitarism. Prostate very small.*

HISTORY: The family history was essentially negative except for a sister, aged 17, who had secondary sex characters, but was quite short and fat and mentally aged about 3. The past history revealed measles, mumps; tonsils and adenoids removed. The patient felt well—*noticed that he had not grown for two years.*

EXAMINATION showed him to be undersized, underdeveloped, slender. His height was 4 feet 6¼ inches; weight, 65½ pounds. He appeared physically to be about eight years old; *genitalis infantile*; no secondary sex characters; *prostate very small.*



Figure 3 (Case 5). 15 years, Lorain type of infantilism—skeletal undergrowth; no prostate felt.

Blood Pressure: 110/75.

Mental Age was 9 years, or *six years retardation*; high grade defective.

The laboratory findings follow.

Urine: Negative.

Blood Picture: Normal.

V. Pirquet: Positive.

Blood Wassermann: Negative.

Spinal Fluid: Negative.

Urine sugar curve: Negative. *Blood sugar curve:* 0.067, 0.135, 0.122, 0.113.

X-ray: Plates of Hands negative. Plate of Skull: Short skull base, small sella, diffuse convolitional markings. Sphenoidal angle 115 degrees.

CASE NO. 5 (See Figure 4). U. C. O. P. D. 380079, W. C., aged 15 years. *Preadolescent Hypopituitarism (Levi-Lorain Infantilism) with Absence of the Prostate.*

HISTORY: Father's family small; mother's family normal. One brother aged 11; four years younger than patient, is larger and taller; one sister aged 7 is normal; one brother aged 3 is normal. Full term, bottle fed, birth weight 8 pounds; walked at 1 year. Whooping cough at age 2. Tonsilectomy at 8. *No growth for 4 years.*

EXAMINATION: Height, without shoes, 46 $\frac{7}{8}$ inches; weight, dressed, 54 pounds (size and height of 8-9 year old). Relaxed inguinal rings. *Penis small; right testis larger than left; can palpate small globus minor and a portion of the body of the epididymus on both sides. The right testicle does not feel like normal testicle—has a tense feeling—both testes transmit light, question of a cystic condition or hydrocele. No pubic hair. Rectal examination: Spinctor tone slightly relaxed; no evidence of prostate. No secretion following massage (note by Doctor L. P. Player, Urologist).*

Mental Age (Binet-Simon): 15 years, very bright, no retardation.

Blood Count: Normal.

Urine: Normal

Wassermann: Negative.

V. Pirquet: Positive to human and bovine tuberculin.

X-ray: Plate of Hands normal. Plate of Skull: Head small, skull thin, sella very small and clinoids almost in contact, accessory nasal sinuses small—sphenoidal angle 150 degrees.

Basal Metabolism: 48.5 per cent plus.

CASE NO. 6. Private patient. H. P., aged 15. Referred by Doctor D. F. Ray, Stockton. *Infantilism; Imbecility; Absence of the Prostate.*

COMPLAINT: Lack of mental, skeletal and genital development.

FAMILY HISTORY: Father living and well, aged 60, no operations, always well. Mother living and well, aged 57, no operations. One sister, aged 30—not strong—teaches—not married—has had several operations—weighs 103 pounds—normally developed. One sister, aged 27—married 2 years—no children—very well—trained as nurse—stout—180 pounds—no miscarriages. One sister, aged 22, not married—115 pounds—well—normal. All did well at school. No dead sisters or brothers. No miscarriages.

HISTORY: Mother went through normal pregnancy with boy—born slightly over 9 months. Forceps used—very long labor. Weighed 12-13 pounds at birth. Other children weighed 8, 8 $\frac{1}{2}$, 9 pounds. *Until he was 2 years old he seemed normal—grew properly—but after that hardly grew at all. First tooth at 11 months—rest came normally. First walked alone at 21 months. Talked before he walked. Measles at 14. Whooping cough at 10, light case. Influenza twice—1918 and 1920. Second time in bed for ten days—for two days temperature 104—first time was lighter case. No other sickness—always well. No operations. No accidents. Always plenty of sunshine and good food and exercise. Mother nursed him until 18 months. Would take only mother's milk. Went to school for three years and was promoted each year—stopped because mother was afraid to have him go alone on account of long way to school. Reads story books. Plays alone at home—does not climb trees. No enuresis. No incontinence. Bowels regular without medicine—appetite good—sleeps well. Has grown very slightly each year—for instance, this last June he grew $\frac{1}{2}$ inch. At age about 10, height 36 inches, weight 36 pounds; at age about 14,*

height 40 inches, weight 40 pounds; at age about 15, height 41½ inches, weight 57 pounds. Weight went up to 57 pounds, October, 1920. He was almost helpless, did not want to move about and a good deal of the flesh was puffy, especially around the neck as if it were air. Then he lost 8 pounds in a month; all this unhealthy flesh disappeared. One month ago he weighed 47 pounds.

EXAMINATION: Weight, 49 pounds (dressed); height, 41½ inches; span, 41 inches; upper measurement, 22½ inches; lower measurement, 19 inches. Peculiarly shaped head, flat and elongated in the anteroposterior diameter, with marked prominence of the occipital region. Face comparatively small. Body is stout over the breasts and abdomen. No hair on lips or chin; no axillary or pubic hair. Ears project like sails. Skin fine and delicate. The six year molars can be seen in x-ray. *Tooth development very backward. Thyroid not felt. Small penis and testicles. Prostate not palpable.*

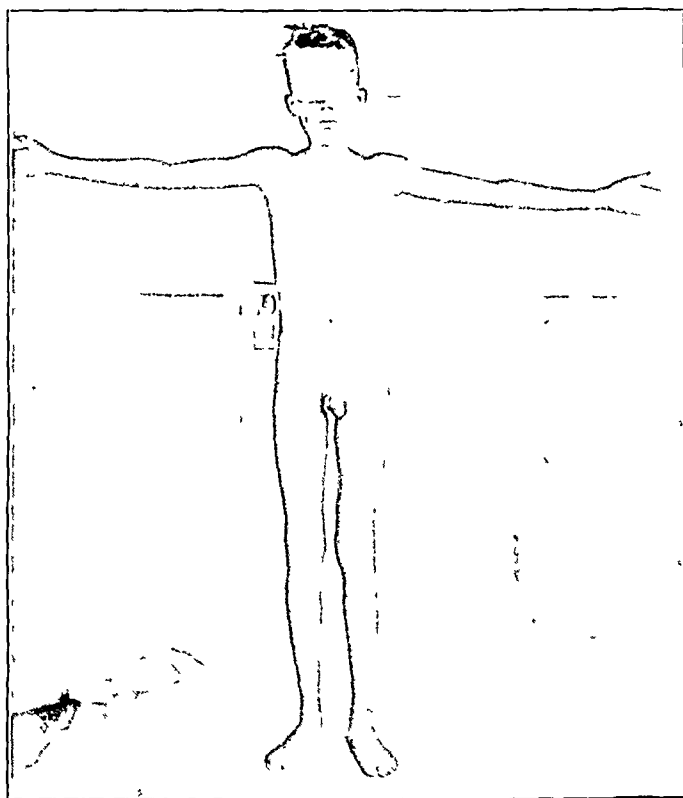


Figure 5 (Case 7) 18 years, Lorain infantilism; slender; no secondary sex characters. Very small prostate

Mental Age (Binet-Simon): 7½ years retardation—Imbecility. Urine: Normal.

Blood Pressure: 80/54.

X-ray Plates both Hands (A. P.)—Thoracic Spine—Lumbar Spine (A. P.)—Chest (Plate)—Skull (Lat.).

The structure of the bones, the size and the epiphyses are about that of a child six years old. (The six year molars are apparent).

The phalanges are broad and short, as are the metacarpals. Six carpal bones are present. Epiphyses are irregular and flattened as in a Perthé disease. There is slight scoliosis. The lung fields are clear. The heart in shape and size is apparently normal for the size of the chest. The skull is flat and elongated in the anterior posterior diameter, with marked prominence of the occipital region. The sella is normal in size, with slight thinning of the posterior clinoids. Sphenoidal angle 145 degrees—acute for his age.

CASE No. 7 (See Figure 5). U. C. O. P. D. No. 66695, boy, aged 18 years. *Levi-Lorain Hypopituitarism with very small amount of Prostate Tissue.*

HISTORY: The patient's mother had numerous miscarriages; uncle had catalepsy. The past history was essentially negative; no ordinary diseases of childhood; tonsils removed twice at the age of 8 and 9 years. There were no complaints except physical underdevelopment.

EXAMINATION showed the boy to be slender, underdeveloped, with muscular and sexual appearance of about 10 years; high pitched voice, *no secondary sex characters*; no hair on face, axillae or pubes; small penis and testes; *very small amount of prostatic tissue barely palpable*. The patient passed all the Binet-Simon tests, even adult, without missing one; there was no mental defect.

The laboratory findings follow.

Blood Pressure: 118/60.

Urine: Negative.

Blood Picture: Normal.

Blood Wassermann: Negative.

Spinal Fluid: Negative.

Von Pirquet: Negative.

Blood sugar curve: .03, .224, .127, .076.

Urine sugar curve: Negative, negative, positive, negative.

X-ray: Plate of Chest: Extensive peribronchial thickening. *Plate of skull:* Sella somewhat small.

CASE No. 8 (See Figure 6). U. C. Hospital No. 10386, H. V. H., aged 21 years. (Seen through the courtesy of Doctor Herbert C. Moffitt.) *Hypopituitarism (atypical Levi-Lorain syndrome) with probable Absence of Prostate.*

COMPLAINT: Lack of physical and sexual development.

HISTORY: One brother, aged 23 years, is over 6 feet tall. No infantilism in the family. Measles, chicken pox; no operations, no accidents; habits good, no alcohol or tobacco. *Normal ten pound baby, developed normally till aged 6 years; since then has grown only about one-quarter inch per year.* Mental development normal; is ambitious and alert; completed 2 years of high school work, aged 19. *Voice has not changed from that of boyhood.* About six months ago a physician gave him x-ray treatments for his thymus, which was supposedly enlarged and relieved him of asthmatic attacks of which he had three or four yearly. Various glandular extracts have been given him without benefit. *Average weight, 60 pounds for many years.* No polyuria or craving for starches or sweets; rarely perspires.

EXAMINATION: *Looks like bright boy of 12 years.* Weight, 64 pounds. Height, 51 inches. Size of a boy of 8 years. Span, 50 inches; upper measurement, 25½ inches; lower, 25 inches. Skin somewhat dry, not thick; *no mustache or beard*; eyebrows thin; a very few pubic hairs have appeared recently; no hair on chest; *mons veneris prom-*

inent, no other fat pads; nails normal; *thyroid not palpable*; no thymic dullness; *penis and testes infantile*; a thin layer of tissue in the region of the prostate possibly represents a rudimentary prostate.

Blood Pressure: 110/80.

Urine: Normal.

Blood: Hb. 75%; R. B. C. 3,904,000; W. B. C. 5200; differential normal.

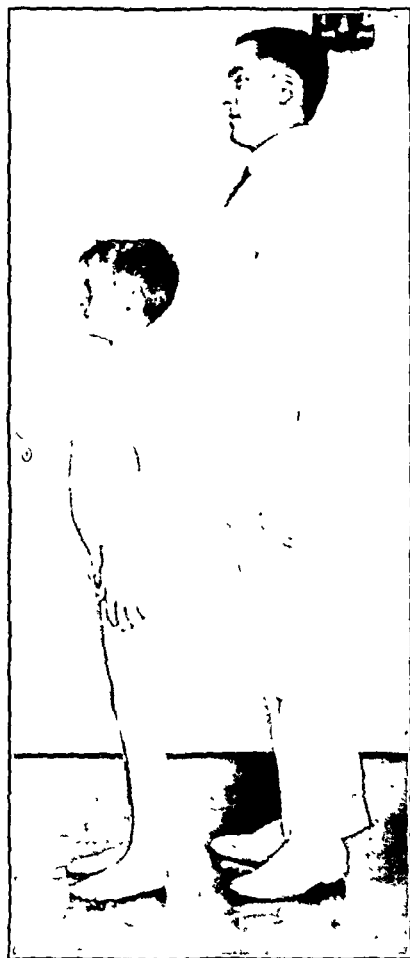


Figure 6 (Case 8). Age 21. Lorain infantilism showing skeletal undergrowth with absence of secondary sex characters. No prostate felt. Normal adult in picture is 5 ft. 7 in. tall.

Stool: Normal.

Wassermann: Negative.

Blood sugar curve: .088, .166, .138, .125.

Urine sugar curve: Negative.

Basal Metabolism: 0.6% below.

X-ray: *Plate of Chest*—Negative except that small bones show delayed development. *Plate of Skull*—Negative; sphenoidal angle 152; third molars show delayed development. *Plate of Arms and Hands*—Epiphyses show development of about 15 years. Long bones are short.

REPORT OF FIVE CASES OF PREADOLESCENT HYPO-
PITUITARISM OF THE FROEHLICH TYPE-
DYSTROPHIA ADIPOSO-GENITALIS

(Prostate absent in four and small in one)

CASE NO. 9 (See Figure No. 7). U. C. O. P. D. No. 66913, R. H., boy, aged 10 years. *Froehlich's Hypopituitarism Associated with Feeble-mindedness and Absence of the Prostate.*

HISTORY: Patient was one of twins, full term; first talked at the age of two and a half years; first walked at three; always fat and heavy; never played with other children; good natured; mentally apathetic, eyes always crossed; could not read; only spoke phrases; no sentences; neither constructive nor destructive; ravenous appetite; sleepy. Measles, pertussis, pneumonia three times; circumcision, ton-

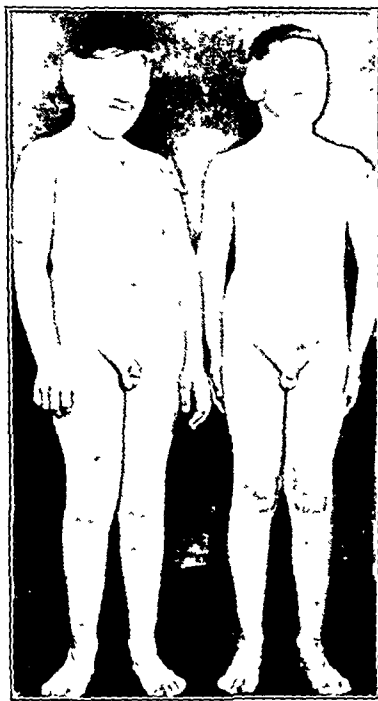


Figure 7 (Cases 9 and 10). Twins, age 10; note feminine configuration—infantile genitalia and adiposity; Froehlich; mental age 3 years; no prostate felt in either.

sillectomy and adenoidectomy. Fat boy with large quadrangular skull, coarse dry hair, female contour, broad pelvis, enlarged mammae, marked mons veneris; female contour of external genitalia, with penis in position of enlarged clitoris, no hypospadias, external genitals infantile; large feet and pudgy hands with marked muscular hypotonicity; tache cerebrale dermatographia.

No prostate was felt rectally. The mental age was from three to four years, or six years' retardation. The laboratory findings were:

Blood Pressure: 118/62.

Urine: Negative.

Blood Picture: Negative.

Wassermann: Negative.

Von Pirquet: Negative.

Blood sugar curve: Fasting 0.103 per cent; one-half hour later 0.129 per cent; one and one-half hour 0.107 per cent; two and one-half hours later 0.088 per cent.

Renal sugar curve: Negative.

Eye fundi: Normal.

X-ray: Plate of Sella and Skull—Negative. Sphenoidal angle 152 per cent.

CASE NO. 10 (See Figure No. 7). U. C. O. P. D. No. 67081, W. H., twin boy, aged 10 years. *Froehlich's Hypopituitarism Associated with Feeble-mindedness and Absence of the Prostate.*

The history, physical examination, mental examination, and laboratory tests were in every respect precisely similar to the findings of the twin brother (Case 9) recorded above, except that Case 10 was fatter, weighing seven pounds more, and being one inch taller and the sphenoidal angle 155 degrees. The figures for the blood sugar curve were 0.116, 0.149, 0.139, 0.106.

CASE NO. 11 (See Figure No. 8). U. C. O. P. D. No. 64092, F. D. L. S., aged 10 years. *Froehlich's Dystrophy Adiposogenitalis, with Absent Prostate.*

HISTORY: Mother (who was mentally aged 8 years) died of sepsis aged 37; history of obesity on mother's side. Full term, normal delivery; breast fed for one year; first tooth at seven months; sat up before one year; walked and talked at one year; measles aged 5 years; mumps aged 8; varicella aged 9 years; patient is second of four children, the oldest being a girl, who is bright mentally and not obese. *Boy was bright up to seven years, since then he has progressively deteriorated; has steadily grown fatter, but no growth in height last three years; has been in first grade in school for three terms without advancement.*

EXAMINATION: *Short, very fat boy; stupid, but good natured and affectionate. Height, 122.5 cm.; weight, 46 kg. (101 lbs.); skin rough and dry with some tendency to scale; mammary glands prominent; abdomen protuberant and very fat, prominent mons veneris; genitals infantile, testes rudimentary; choreiform movements of both arms, more marked by motion and when attempting to grasp anything.*

Rectal Examination: *Possibly tiny rudimentary prostate but almost impossible to be sure by palpation whether a prostate is present or not (Doctor Frank Hinman).*

Mental Age: 4 years—6 years retardation.

Blood Count: Normal.

Von Pirquet: Negative.

Wassermann: Negative.

Urine: Normal.

Blood sugar curve: .102, .119, .115, .099.

Urine sugar curve: Negative.

Chest Screen: No evidence of thymus.

X-ray Plate of Skull: Small sella, sutures permanently closed.

CASE NO. 12 (See Figure No. 9). Private case, B. B., aged 10½ years. Referred by Doctor Frank Hinman. *Preadolescent Hypopituitarism (Froehlich's Dystrophy Adiposogenitalis) with tiny testicles and barely palpable prostate.*

COMPLAINT: Obesity and sexual infantilism.

HISTORY: Father living, aged 45, has diabetes—no other diabetes in family. Weight. 200 pounds; height. 5 feet 10½ inches; looks very

young; is stout. Mother living, aged 51 (had all teeth removed, has rheumatism); weight, 203 pounds; height, 5 feet 7 inches. Very stout. Father's father weighed 250 pounds. Mother has two brothers, one being 6 feet 4 inches in stocking feet, weight 200 pounds; the other 6 feet 1½ inches in stocking feet and weighs 180 pounds. Has three sisters all six feet tall. Mother married before at 18 to a man 20 years older than herself. First husband died of typhoid fever 6 years later. Had four children in those six years. One son is living. One daughter died at 10½ months. One boy died of spasm at 9 months—hands very tiny. One child died at birth. Was a widow for four

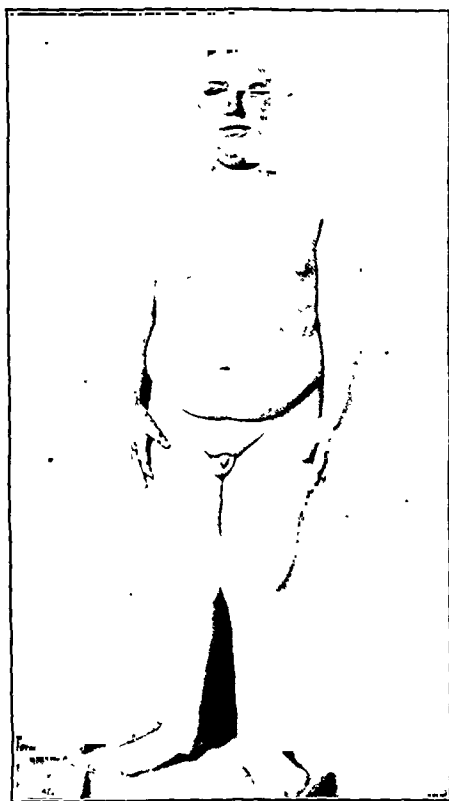


Figure 8 (Case 11). Age 10—mental age 4. Froehlich type; no prostate felt.

years. Married to second husband 23 years age at 28. During first twelve years was not pregnant, but wanted to be. Then came patient. Two years later had daughter, now aged 8. No other pregnancies or miscarriages. The daughter is quite normal. Boy was born at full term, without instruments, normal birth. *Mother nursed him to 15 months*—would not be weaned. Began to walk at 9 months without assistance; had two teeth at 4 months and others followed regularly. Started to talk at 1½ years. Read at 5 years—was determined to learn to read—mother taught him. At 4 family noticed that he was nervous—could not keep his feet still; then slept from 2 P. M. to 9 A. M. next day and then could not lift feet—could not walk—dragged

both feet—then shuffled along. Ever since the age of 4 has had nose bleeds, sometimes lasting two hours before it would stop. Has them in spells every week or two—was circumcised at 2 weeks and doctor called him “a bleeder” at that time. He was quite well until June, 1921. He has had severe *headaches* for years, always on right side, mostly temporal region; these occur one to three times a week. Will fall to sleep for many hours, wake up and vomit (not projectile); sees colors and things dancing before his eyes; headache slightly better when he lies down—is heavy and hot in head. Been nervous for years—good disposition. Appetite large—likes bread, but not potatoes or sweets. Bowels somewhat constipated. Sleeps well, snores, no nocturia, some-

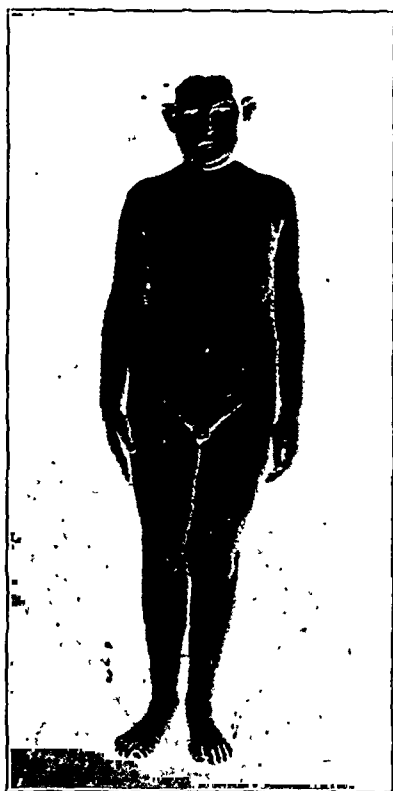


Figure 9 (Case 12). Age 10½ years; Froehlich type; adiposity and sexual infantilism; no prostate felt.

times is very thirsty. Passes considerable urine. No incontinence. Was normal size until 9 months ago—then he began to get stout. Gained about 35 pounds in past 9 months (121 dressed now). Eats only two meals a day. Gets along well with other boys—good scrapper—and plays hard. Was hit over the head with a willow pole on left temple at 7. He has never had any convulsions. Boy reads a good deal. He is in the fourth grade—went to school when he was 7½ years of age. School work is satisfactory.

EXAMINATION: Fat boy with *considerable mammary development*, fat hips and abdomen with feminine contour, and *prominent mons veneris*. Height, 58 inches. Weight, 113.52 pounds stripped. Span, 60 inches. Upper measurement, 29¼ inches; lower, 28¾ inches.

Doctor Frank Hinman reports—*Very small penis, small testicle*

on one side and barely any on the other, and prostate barely palpable.

Mental Age (Binet-Simon): 12 years—1½ years ahead.

Blood: R. B. C. 5,118,000; W. B. C. 8400; Hb. 66%; differential—normal.

Blood sugar curve: 0.078%, 0.125%, 0.126%, 0.139%.

Urine sugar curve: Negative.

X-ray Plate of Skull: Sphenoidal angle 145 degrees. The calvarium is large and thin and shows no abnormal markings. The sella is within normal limits. Large sphenoidal sinus and antrum.

Basal Metabolism: 27.3% plus.

CASE No. 13 (See Figure No. 10). Mr. A. C. R., private patient, aged 47 years. *Froehlich's Syndrome with very small Prostate.*

HISTORY: The father's age was 53 and the mother's age was 43 when patient was born. One brother shaves very rarely, the other

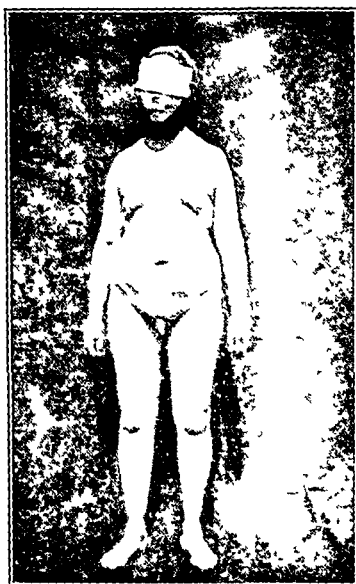


Figure 10 (Case 13) 47 years, note adiposity with feminine configuration of the thighs prominent mons veneris, mammary glands, female type of pubic hair, tiny genitalia, prostate very small

does not shave at all; both brothers are married and have children. The patient has two sisters; one is married and has children. He had measles and mumps as a child; influenza in 1890; typhoid at 37. He has been married 15 years; the wife is well; there have been no pregnancies. In the past four years he has had peculiar fainting spells, usually associated with emotional excitement; there have been no convulsions; he does not bite his tongue or have incontinence of urine or feces.

EXAMINATION: Weight, 185 pounds; high pitched voice; cheeks, chin and upper lip entirely devoid of hair (he has never shaved); body of characteristic feminine contour with abnormally developed breasts; prominent mons veneris and typically feminine hips and thighs; the pubic hair is somewhat scanty. The external genitalia are infantile, resembling those of a boy of eight; the testicles are decidedly small.

246 ABSENCE OF PROSTATE AND ENDOCRINES

Prostate is easily palpable, but much smaller than normal. He has never obtained satisfaction from sexual intercourse. The skin is dry and never perspires; the thyroid is slightly enlarged. He says he had a goiter 12 years ago which was painted with iodine twice a day and disappeared.

Blood Pressure: 110/75.

Urine: Normal.

Blood Count: Normal.

X-ray Plate of Sella: Sella small; sphenoidal angle 162 degrees.

Basal Metabolism: 26.4% below normal.

REPORT OF TWO CASES OF DYSFITUITARISM (GIGANTISM AND INFANTILISM, NEURATH-CUSHING TYPE)

Prostate very small in both

CASE NO. 14 (See Figure No. 11). M. G., aged 31 years. (Inmate No. 34307 of California State Prison at San Quentin—seen through the courtesy of Doctor L. L. Stanley, Resident Physician.) *Dys-*

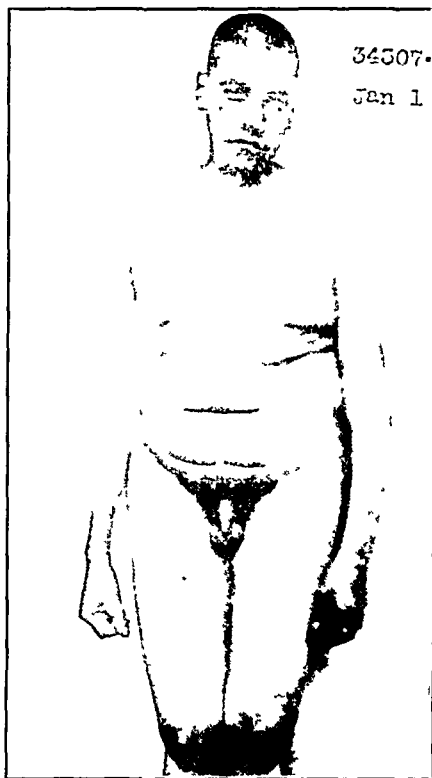


Figure 11 (Case 14). Age 31; gigantism and infantilism; feminine fat distribution; female type of pubic hair, testes and prostate very small.

pituitarism with Infantile Genitalia and Tiny Prostate (Neurath-Cushing Type).

HISTORY: Born in Spain, laborer, not married; was an only child; always well except gonorrhoea for three weeks at 19; fracture of leg at 26; *was fully grown (over 6 feet) at 17*; was active and energetic when working in mines from 11 to 16; *of late years has tired easily*

after walking or a small amount of work; has noted dyspnoea on exertion; *has never shaved more than once a week*; and sometimes has not found it necessary for several months; says testicles were larger at 20 than now. Was insulted about sexual habits, it being insinuated that he had intercourse with boys, fight ensued and he killed his opponent in self-defense; is in jail for manslaughter.

EXAMINATION: Tall, burly, heavy build; weight about 200 pounds. Low forehead, *fat mammary glands* with large nipples and fat lumbosacral pads; face dry and senile, neck thick, hands large; *very little hair on face or axillae, pubic strictly feminine*; skin dry and smooth; *penis small, scrotum small, testes small, prostate very small*. Wassermann negative.

CASE NO. 15 (See Figure No. 12). L. Z., O. P. D. No. 73098, aged 51 years. *Gigantism and Infantilism with Very Small Prostate.*

HISTORY: The patient's height is 6 feet and the weight 250 pounds. No other member of the family, including the mother and

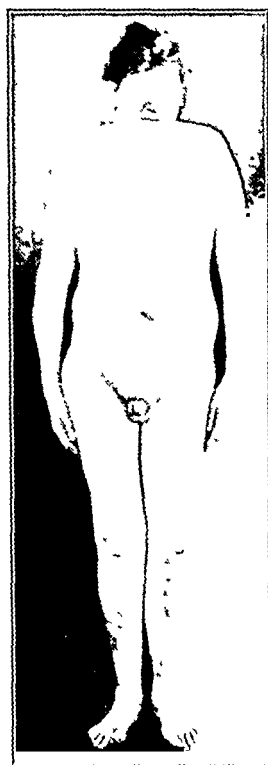


Figure 12 (Case 15). Age 51; gigantism and sexual infantilism; prostate very small.

four brothers, have any similar disturbances. The past history is unimportant. The patient noticed that he was different from other boys because they poked fun at him on account of his large breasts and small genitals. He has never shaved. The voice is high pitched. He had never had any sexual desire, erections or intercourse. He was tall for his age and as a boy was fat. He was 6 feet tall at 16 years. He

was always very strong and powerful; being sensitive about not being like other men he sought always very strenuous physical labor, such as that of a sailor; he did deep water diving. His case in 1914 was diagnosed by Barker at Johns Hopkins as "acromegaly and infantilism." At that time he had excruciating headaches with explosive, projectile vomiting. Cushing and Horrax of Harvard saw him in 1917, and because of vomiting and headaches, a decompression was done, apparently a subtemporal, which relieved the headaches and vomiting almost immediately and he has had none since. Rigdon and Stanley performed a transplantation of human testicle into the scrotum in December, 1919. He was demonstrated in 1920 at the California State Medical Meeting in Santa Barbara. He had several erections within 24 hours following operation, the first he had ever had in his life; the transplant did not slough, but gradually atrophied; three months following the operation he had intercourse successfully twice. There had been no hair whatever on his face prior to the transplantation, but it began to grow about a month later and can be seen in present picture; he has never shaved; he wants to grow a beard. There has been no hair between umbilicus and symphysis until recently; there is some present now and also some pubic hair. Although he formerly never perspired, the skin has become smooth and moist. While he was with Barker in 1915, *the prostate was searched for and only a very small organ was found.*

REPORT OF THREE CASES OF EUNUCHOIDISM

(Prostate absent in all three)

CASE No. 16 (See Figure No. 13). U. C. O. P. D. No. 80944, N. P., aged 43 years. *Eunuchoidism with Absence of the Prostate.*

COMPLAINT: Palpitation, weakness and loss of weight.

HISTORY: Family history negative. Whooping cough at 12; mumps at 23; smallpox at 25; typhoid at 35. No operations. Best weight 180 pounds; average weight 165; present weight 156 pounds.

Present Illness: Aged 10 was teased by playmates because of small genitalia. Aged 14 secondary sex characters developed. Shaved at 15. Attempted masturbation without success. Never attracted to women. *Tried intercourse on three different occasions without success—never has had erection.* In 1916 at Cook County Hospital was informed that he had no testicles. July, 1921, while working in cyanide extracting plant, began to have palpitation with nausea—no vomiting. Weakness and great fatigue came on. Was examined by company physician and told to leave work because of chronic cyanide poisoning. Also advised extraction of abscessed teeth. Thereupon had 15 teeth extracted followed by temporary improvement.

EXAMINATION: *Apathetic, listless manner.* Height, 67 inches; span, 72 inches. Upper measurement, 33 inches. Lower measurement, 34 inches. Weight, 153½ pounds (dressed). *Peculiar, pasty, fawn-colored skin with innumerable fine wrinkles, especially around the mouth, nose and eyes.* Hair rather coarse on scalp and extremely bristly beard. Axillary hair sparse, *pubic typically feminine distribution.*

Lungs—dullness at both apices but no rales or pathological breath sounds.

Genitalia—*testicles atrophic and transmit light, epididymis normal, prostate not palpable.* Mons veneris present.

Blood Pressure: 95/60.

Temperature: At 10 A. M., 96.8 degrees.

Urine: Normal.

Blood Count: Normal.

Phthalein: Total 2 hours, 50%.

Wassermann: Negative.

Gastro-intestinal Screen: Negative.

Screen of Chest: Negative.

X-ray: Plate of Teeth—One root abscess and pyorrhoea. *Plate of Skull*—Sella normal. Sphenoidal angle 153 degrees. *Plates of Hands*—Normal.

Basal Metabolism: 4.7% plus.

Electrocardiogram: Bradycardia—rate 50. P-R interval 6/25 second., definite A-V block. Otherwise within normal limits.

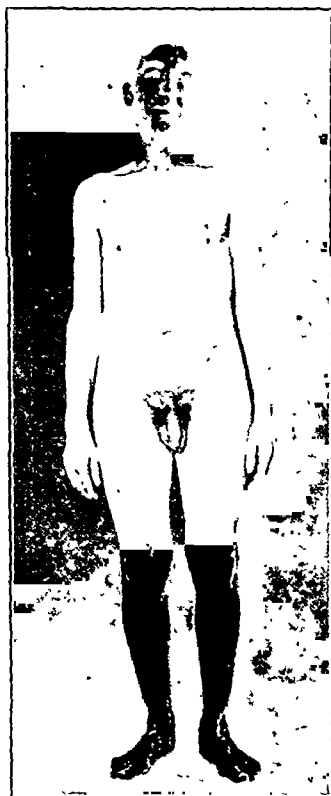


Figure 13 (Case 16). Eunuchoidism: 43 years; female type of pubic hair; long arms and legs; atrophic testicles; prostate not felt.

CASE No. 17 (See Figure No. 14). U. C. O. P. D. No. 64936, L. C., aged 31 years. *Eunuchoidism with Absence of the Prostate.*

HISTORY: Family history unimportant. Past history unimportant. Eleven years ago genitalia were injured in an accident. Was treated by injections through penis, which resulted in swelling testicles to size of baseball; left testicle then broke down and drained for short time; then both testicles shrunk and atrophied.

EXAMINATION shows asthenic emaciated individual, wretched posture. Left testicle palpable, but small and soft, epididymis intact; right epididymis somewhat indurated but testicular substance almost entirely absent. Rectal—*no vesicles or prostate can be palpated; no*



Before Injury to Testicles

1. Bright and alert, vigorous and strong.
2. Shaved every other day.
3. Hair on chest, arms and legs and pubic copious.
4. No itching.
5. Libido and potentia active.
6. Weight 126 pounds.
7. Nails normal.

After Injury to Testicles

1. Mentally sluggish, physical inertia.
2. Shaves once a week.
3. No hair on chest, arms or legs, and pubic hair is definitely feminine in type—axillary scant.
4. Fruritis ani with fissures and cracks.
5. Libido less but still fair, potentia present but decreased.
6. Weight 105 to 109.
7. Nails show onychchauxis.

Figure 14 (Case 17). Age 31 years; eunuchoidism following injury to testicles; prostate not felt.

secretion obtained after massage; no secretion seen in urine voided after massage.

Urine: Trace of albumen, otherwise normal.

Phthalein: Total 2 hours 60%.

Wassermann: Negative.

X-ray Plate of Chest: Subacute inflammatory process—not tuberculous.

Stool: Normal.

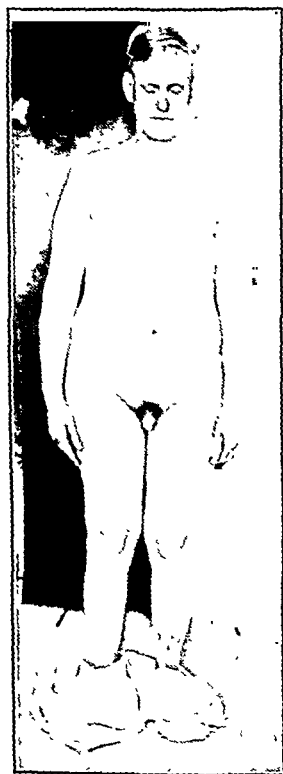
Blood Pressure: 98/68.

Blood Count: Secondary anemia.

CASE No. 18 (See Figure No. 15). U. C. O. P. D. No. 72976, C. K., aged 47 years. *Eunuchoidism with Absence of Prostate.*

HISTORY: Family history unimportant. Measles, mumps, chicken pox, tonsillitis in childhood; typhoid aged 30; malaria slightly aged 37; influenza with pneumonia in 1918 epidemic, in bed 30 days; pneumonia 1917 also; Neisser and Chancre with secondaries aged 20. Following the influenza pneumonia of 1918, heart symptoms of dyspnoea, palpitation and weakness appeared, for which he came to the clinic. While in University Hospital had an attack of paroxysmal tachycardia which was caught on the electrocardiograph (rate 220 per minute). Pulse rate ordinarily 50 to the minute. Evidence of mitral insufficiency and stenosis and myocardial insufficiency was found.

Nine years ago fell and injured right testicle, which became swollen and had to be removed. The left testicle atrophied soon afterward.



Before Injury to Testicle

1. Full of life and vigor, sociable, quick thinker, excellent memory, self-confidence.
2. Marked libido and potentia.
3. Hair on chest, abdomen, arms and legs.
4. Penis large.
5. Slender, pubic fat normal.
6. Skin smooth, elastic, firm.
7. Voice strong and deep and speech clear and distinct.
8. Eyesight and hearing excellent.

Since Injury to Testicle

1. Quiet, dull, no energy, poor memory; gropes for words and thoughts, nervous and irritable.
2. No libido and very rarely has an erection.
3. No hair on arms, legs or chest, and pubic hair is of feminine type.
4. Penis small, almost infantile.
5. Fat, especially mammary; abdomen and hips like female, and mons veneris prominent.
6. Skin dry and thin, and finely wrinkled.
7. Voice weak, but not high pitched, and speech blurred.
8. Eyesight and hearing poor.

Figure 15 (Case 18). Age 47—eunuchoidism following injury to testicles; obese type resembling the Froehlich but due primarily to gonad deficiency rather than pituitary deficiency; prostate not felt.

EXAMINATION as indicated above; scrotum almost gone, very small left testicle, consisting principally of epididymis and not much of that. Right testicle gone. *No prostate palpable per rectum.*

Blood Count: Hb. 65%; R. B. C., W. B. C. and differential, normal.

Urine: Very slight trace of albumen—otherwise normal.

Blood Pressure: 70/40 (prone).

Wassermann: Negative.

X-ray: Plate of Chest—Mitral heart. *Plate of Skull*—thick calvarium, sphenoidal angle 145 degrees.

Basal Metabolism: 12.9% below.

DISCUSSION

1. The prostate does not develop if castration is performed early in life.

2. The prostate though normally developed will atrophy and eventually disappear if castration is performed in the adult.

3. Castration has no effect on hypertrophied prostates.

4. In hypogonadism or eunuchoidism the prostate atrophies.

5. Goetsch showed that feeding anterior lobe pituitary to young rats hastens the development of the prostate.

6. Many investigations have shown that experimental hypopituitarism is followed by sex infantilism, including retarded development of the prostate.

7. In clinical hypopituitarism in the male the prostate fails to develop, if the disease starts before puberty, and atrophies if the hypopituitarism has its onset after puberty.

Not much is to be gained at this time by elaborating theories concerning absent or diminutive prostate in hypopituitarism. It is established that atrophy of the prostate occurs after castration; we also know that testicular aplasia occurs in hypopituitarism. Whether the prostatic aplasia or atrophy in hypopituitarism is due directly to the lack of pituitary secretion or whether it follows upon testicular insufficiency is difficult to decide. As it happens all the cases that show absent or diminutive prostates likewise show small and insufficient testes.

CONCLUSIONS

1. There are herewith reported 15 cases of hypopituitarism (8 of the Lorain type, 5 of the Froehlich syndrome and 2 of the Neurath-Cushing type) and 3 cases of primary gonad deficiency. Of the 18 cases, no prostate could be felt in 13 cases and only a diminutive organ in the remaining five.

2. The prostate is large enough normally in childhood to be easily felt, and pediatricians especially are urged to make rectal examinations in boys who show stigmata of infantilism.

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THE DIAGNOSIS AND TREATMENT OF THYROID DISEASE AS CONTROLLED BY THE METABOLIC RATE*

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The metabolic rate of an individual indicates the rate of the heat production or energy transformation resulting from the chemical changes going on in the body when at complete physical and chemical rest. Metabolic rate studies, especially, have increased our knowledge of thyroid diseases. They have been the means of distinguishing hyperthyroidism from psychoneuroses, the exophthalmos of Graves' disease from congenital eye prominence, toxic from non-toxic adenomas, and hyperthyroidism or myxedema from obesity and other conditions resembling such disturbances. The rate, when abnormal, means, in the absence of certain definite diseases and inanition, a disturbance of thyroid secretion.

The metabolic rate studies, moreover, have afforded an opportunity to check up on the contention of Goetsch that his epinephrin test, when positive, indicates hyperthyroidism. It is now generally accepted that there can be no hyperthyroidism without an increased metabolic rate and since Peabody, Sturges, Tompkins, Wearn and others have shown that Goetsch's test is not even constant in true hyperthyroidism and may be even positive in hypothyroidism, neurasthenia, and in normal individuals, "it cannot be regarded as having any specific significance in the diagnosis of hyperthyroidism."

The dependability of metabolic rate determinations has increased gradually in the past few years because of the study of normal values by such investigators as DuBois, Benedict, Carpenter, Talbot, and Dryer. Means and Woodell in 1921 analyzed results obtained by the respective standards of DuBois and Aub, Benedict and Harris, and Dryer, and concluded that the deviations among the three are slight, and that the DuBois standards should continue to be used. Last year, we also published an analysis of the results obtained by the DuBois and Benedict

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methods and showed that when a normal value for every year is used, these being calculated from the DuBois tables instead of using his values, which are for each decade, that the results obtained from such standards and from Benedict's tables are practically identical. Our investigations, moreover, indicate a normal rise in the metabolic rate with menstruation, in confirmation of similar results obtained by Rowntree. Though criticism of such a possibility has occurred, until the question has been thoroughly investigated a premenstrual determination should not be relied on as indicating the average-day-to-day rate.

TECHNIC AND INTERPRETATIONS

After some 600 tests on 316 thyroid suspects and many normals, we feel it most important to perform the metabolic test with the greatest care and accuracy. Peabody states the drawback of the test is that it requires skill even with simplified apparatus. With the apparatus and technic used, normal results must be obtainable on normal individuals as recently emphasized by Jones. Patients must be at absolute rest, in complete relaxation. This is most important, as shown by the gradual increase in the rate of a patient who could not relax. Three separate determinations were made, the results in order being plus 24 per cent, plus 29 per cent, and, finally, when the patient was extremely worked up over the test, the result was plus 37 per cent. Some patients cannot cooperate and remain relaxed over long periods of time, and dependable metabolic rate determinations on such individuals are difficult to obtain. If the final result is plus 10 per cent to plus 20 per cent or minus 10 per cent to minus 20 per cent, it is important in order to rule out error in technic to repeat the test before deciding by means of the result alone on a disturbance in the metabolic level. The normal outer limits of basal metabolic rates are given as plus 10 per cent to plus 15 per cent, though unquestionably certain slight or early disturbances are indicated, at times, by such rates. The pulse rate, moreover, must be studied carefully, since it is certain that a resting pulse rate below 80 or even 90 is rarely associated with an increased metabolism, which fact was emphasized by Sturges and Tompkins in 1920. The temperature curve also should be known, and certain diseases, other than thyroid disturbances, which are known to cause abnormal metabolic rates, must be

ruled out. Thus it is important that the rate be determined and interpreted with care and along with a painstaking diagnostic study.

An accurate metabolic rate determination and interpretation, therefore, depends on so many factors that I feel these tests *should be made under the supervision of or by a clinician who is in touch with the clinical problems of thyroid disease.* The report of the rate should be supplemented by such a physician's clinical opinion. A technician or the physician who sees only an occasional thyroid case, is unable as accurately to judge the reliability of a report as is the clinician who is paying special attention to thyroid disease.

As to choice of apparatus, the modified Tissot unit, as we have pointed out before will give the most accurate results because the respiratory quotient is estimated for each individual patient. The method recently described by King of Johns Hopkins also appeals to me. King estimates the basal rate by the determination of CO_2 alone. But for clinical investigation one of the so-called portable instruments which estimates directly the amount of oxygen consumed by the patient is at this time to be recommended. Roth recently advises the substitution of valves for the motor in the so-called Benedict's "New Portable," and his results as well as the simplicity of the technic seem highly satisfactory. He also advises the use of a kymographic tracing to record oxygen consumption as well as the type of respiration, instead of depending on direct readings of the fall of the spirometer bell. He points out that basal conditions brought about by the preliminary 30-minute rest period are usually disturbed at the start of the test, as definitely shown on the graphic curve, and thus advises discarding that part of the curve, which does not represent the probable metabolic rate. With this method, no spirometer readings or stop watches are necessary, and Roth claims the procedure is reduced to great simplicity. He also suggests the use of "Natron Soda" or a combination of "Wilson soda lime" with a thin upper layer of anhydrous calcium chloride so that the error of from plus 1 to plus 3 per cent introduced because of the moisture content of the air can be eliminated.

PATHOLOGY OF THE THYROID

It will aid in the discussion of the subject if we review our present knowledge concerning the pathology of the thyroid gland.

Plummer has done much to simplify the pathology of goiter by pointing out the fact that only three common types of non-malignant enlargements occur, the colloid, the adenomatous, and the hyperplastic goiters. His contention that the goiter of adolescence is either adenomatous or colloid in type, such enlargements resulting from sustained stimulation of the thyroid in the presence of a deficiency of available iodine, seems reasonable. The colloid and especially the adenomatous goiters, may undergo various degenerations, such as cystic, hemorrhagic, or calcareous, and mixtures of all three types may occur. These degenerative changes as well as the mixed goiters explain the confusion which exists in the usual treatises on pathology, and it is thus refreshing to be able to analyse goiters by Plummer's simplified classification.

The colloid goiters are supposed to result from an excessive stimulation of the thyroid in the presence of a lack of assimilable iodine in food and water. The thyroid parenchyma under such conditions may overfunction, secreting excessive colloid in an effort to compensate for the deficient iodine. McCarrison offers evidence, moreover, pointing to the probability that diffuse colloid goiters are due to infection, and Plummer feels that this infection may be in the intestinal tract, making the proper absorption of iodine from food and water impossible. This would explain why iodine given by mouth in certain cases of diffuse colloid goiter is not absorbed.

The adenomatous thyroid results, as is well known, from a growth of embryonal interstitial cells without participation of the parenchyma of the gland. New acini may form and if they form no colloid, they are called fetal adenomas; however, if colloid forms within the acini, they are called adult adenomas, and the acini of this adult type may become indistinguishable from the normal thyroid tissue. The adenomatous tissue may be encapsulated or diffuse. When encapsulated this type may be single or multiple and they form the true adenomas of the thyroid, giving rise to the largest types of goiter and being very subject to degeneration. The tissue outside the adenoma may be normal or may contain colloid or hyperplastic areas, thus giving rise to a mixed type of goiter. The unencapsulated adenomatous tissue gives rise to the so-called adenomatosis of the thyroid.

There are certain nodular colloid goiters as well as isolated hypertrophic areas in certain thyroids which, on examination, bring up the question of a relationship to adenomatous tissue. Plummer feels that both of these conditions have their origin in adenomatous rests and points out that all may give rise to hyperthyroidism, different, however, from that resulting from a diffuse hypertrophic gland. He states, moreover, that some hypertrophy of the cells of acini is present in most adenomata. It is interesting to mention that no good explanation of why an adenoma begins to secrete thyroxin and thus produce hyperthyroidism years after the adenoma first forms offers itself, and Mayo recently stated that the pathology of toxic and non-toxic adenomata does not differ.

The thyroid in true exophthalmic goiter uniformly shows generalized primary parenchymal hypertrophy and hyperplasia. This may be in an early, advanced, or regressive stage. In the early stage, the single layer of cells lining the acini become columnar and colloid diminishes. Papillomatous-like masses of hypertrophic cells soon project into the acini and in advanced stages the acini become completely filled with these cells and the colloid disappears. In this stage, therefore, thyroxin is being secreted very rapidly and, since colloid is supposed to hold thyroxin and regulate its absorption, this secretion is being absorbed overly fast. The last stage may result from self-destruction of the parenchyma due to overfunctioning of the hyperplastic tissue or to surgical ligation of the thyroid arteries. In the advanced stage the gland is apt to be very vascular. The enlargement in exophthalmic goiter is usually uniform, though it may be unilateral, and it has an elastic, slightly granular feel.

Goetsch describes a pathologic condition in which there is a "marked hypertrophy and hyperplasia of the interstitial cells of the thyroid with an atrophy of the normal parenchyma." He says the gland may not be enlarged at all. The symptoms, he claims, are those of a toxic adenoma and many of these patients have been treated for tuberculosis. However, the metabolic rate is not increased and the general opinion is that Goetsch is mistaken in his opinion that the symptoms are due to thyroid overactivity. There has been no definite confirmation, moreover, of his pathological findings. We feel that certain of these cases he describes are early cases of hyperplastic goiter which would

show an increased metabolic rate if a careful test were made. In spite of Goetsch's contentions, all evidence points to the conclusion that there can be no hyperthyroidism without an increase in metabolism.

Malignant tumors of the thyroid will not be discussed except by stating that they may be carcinomatous or sarcomatous. Moreover, the adenoma may be proliferative in type, penetrating the capsule and metastasizing. Wilson, in 1921, published an excellent article on malignant tumors of the thyroid.

In primary hypothyroidism, the thyroid gland becomes atrophied or converted into a fibrous mass. In 100 cases, Mayo states that thyroiditis was the etiological cause in two-thirds of them. In mild cases of hypothyroidism, pathological changes may not be marked. Hypothyroidism, as is well known, may follow hyperthyroidism or may result from pressure atrophy of normal thyroid tissue brought about by adenomatous nodules or in diffuse colloid enlargements.

CLINICAL VALUE OF BASAL METABOLIC STUDIES COLLOID GOITERS

Basal metabolism studies are of importance in the study of certain colloid goiters. Neurotic individuals who have goiters of this type may present all the symptoms of toxic adenoma, and to be sure that a mixed form of goiter containing either hyperplastic or adenomatous tissue is not present, a test of this nature must be used. Early colloid goiters may be reduced by the administration of small doses of iodides or thyroid extract, and when such colloid is made to disappear, small adenomatous nodules can at times be palpated. Colloid goiters with lateral lobes 6 cm. or more in diameter have been found by Plummer to have a metabolic rate of minus 6 to minus 18 per cent, but apparently never yield a hypothyroidism of greater degree. Such goiters, due to probable compression of their parenchymal cells, are unable to yield enough thyroxin for the demands of the body. Plummer has found that an intravenous dose of 5 to 10 mg. of thyroxin will lead to diminished bruit, thrills, palpability of arteries and size of the colloid goiter within 24 hours, and states that even the largest colloid goiters will disappear in 8 to 12 weeks. If such does not occur, the struma may contain adenomatous tissue. The metabolism of these cases of colloid goiter must

be kept at, or slightly above, normal for some weeks until the struma is well decreased in size. Thyroid may be given by mouth if absorbed; otherwise thyroxin should be given by vein and the metabolic rate determinations must be the guide.

ADENOMAS

Adenomas of the thyroid are the cause of the largest percentage of goiters in adults. Careful routine palpation of the thyroid will reveal a large number of small adenomatous enlargements, of the presence of which the usual patient is unaware. Adenomas begin to develop in the twenties and early thirties, and a certain percentage of them produce toxic symptoms on an average of 14 or 15 years afterwards. However, if iodine is given with the idea of causing a decrease in the size of early adenomata, such tissue will often begin to secrete thyroxin and thus produce a permanent hyperthyroidism. These toxic adenomas produce a very typical syndrome which Plummer described in 1911 and 1912 as toxic non-exophthalmic goiter, and which has lately been termed Plummer's disease. Boothby recently pointed out that before Plummer's article this disease caused much confusion in the literature on toxic goiters and many names, such as goiter heart, Basedowoid, formes frustes, and others, were suggested for it. This condition is characterized by "nervousness, tremor, tachycardia, loss of weight and strength, and a tendency to hypertension. In the later stages, myocardial disintegration appears." The cause of adenomatous thyroids taking on the property of over-secretion of thyroxin is not known, and the intoxication caused by toxic adenomata is probably a true hyperthyroidism and different from that due to exophthalmic goiter, in which disease the thyroxin molecule is assumed to be different from the normal thyroxin. Plummer feels that the adenomatous tissue actually secretes colloid and thyroxin and stores iodine. Because of the insidious onset and the possibility of a long, low grade intoxication which is a special degenerative influence on the myocardium, it is not definitely to recognize the disease. As a definite diagnosis, nothing is of as great value as the determination. A recent case emphasizes the clinical taint in former diagnoses, and the rapid cure

which is possible by careful diagnostic and metabolic studies and surgical treatment.

W. W., a man of 45, has been underweight for about seven years. He has been unable to make a gain in spite of extra nourishment. He thinks he is lacking slightly in energy and ambition and is definitely warm blooded. For several years he has perspired easily at night and his wife has feared tuberculosis because of his general symptoms. Physical examination showed a thin, nervous acting man, with rather moist skin. His pulse rate was 80. Blood pressure was 130-80. Heart was slightly enlarged to the left and an old apical systolic murmur was present. Palpation of the thyroid revealed the presence of a walnut sized adenoma which was not visible and had never been noticed by any of several physicians who had looked him over recently. No eye signs were present. The metabolic rate was plus 35% on one occasion and plus 37% three months later. Surgical enucleation of the adenoma was easily accomplished, recovery was rapid, and within two months 25 pounds had been gained and the nervous patient transformed into a quiet, healthy individual.

Another case illustrates the possibility of blaming the weakened myocardium for symptoms really due to a toxic adenoma.

W. B., a man of 50, has for several years been short of breath so that now he is unable to do any physical work. He has been told for several years that his heart is weak. He has no edema and no cough. On questioning, he gave the history of nervousness, weakness, tachycardia and tremor, especially in the legs. Physical examination revealed a small walnut-sized adenoma. No eye signs were present. Fluoroscopy showed a moderately dilated heart. Pulse rate was 90. Blood pressure was 118-80. The metabolic rate was plus 44%. The patient was skeptical of my diagnosis and disappeared from observation. This adenoma had probably been toxic for several years, which toxicity gradually was producing myocardial degeneration as evidenced by his increasing dyspnea.

The importance of the studies of Plummer in this disease cannot be overemphasized, since this difficulty is comparatively common. Moreover, the possibility of recognizing the early cases has been made possible through metabolic rate determinations. In the future, therefore, we should be able to prevent the long invalidism and the myocardial degenerations which have heretofore gone unrecognized for years, as shown in the two cases cited above. Basal metabolic rate studies are especially important in the investigation of adenomas of the thyroid in psychoneurotic patients, since it is especially important to know if such adenomas are toxic. Moreover, a mild hypothyroidism which at times results from pressure atrophy of the normal thyroid

parenchyma, due to several large adenomata. can be discovered by metabolic rate studies. If a rate of over 50 per cent is obtained in a goiter, one must suspect the possibility of hyperplasia as well as adenomata, since the average rate of toxic adenomata is around 32 per cent. In the absence of exophthalmos, it is always to be remembered that hyperthyroidism as shown experimentally by an increased rate, may be due to a diffuse unencapsulated adenomatosis. In these ways, therefore, the metabolic rate is of value in the diagnosis of adenomata.

Moreover, in the treatment of toxic adenomatous thyroids, the metabolic rate will tell whether surgery, for example, has enucleated the single tumors successfully, or resection of gland tissue in the diffuse adenomatous type has been extensive enough. Whereas, the general opinion at present is that surgery is definitely indicated in all cases of Plummer's disease, Holmes recently has reported several cases of adenoma cured by x-rays. and Tyler says that this type of goiter responds better to x-ray therapy than does the exophthalmic type. We have had a recent experience in which, by mistake, an adenomatous thyroid was given x-ray treatment with a practical disappearance of the nodule and a reduction of the metabolic rate from plus 55 per cent to plus 5 per cent in two treatments. The thyroidism, however, has returned and we are continuing the use of x-rays. Another case of a toxic degenerated adenomatous thyroid was treated for eight months with x-rays without any result at all except an increase in the patient's rate from plus 55 per cent to plus 64 per cent. We still feel that adenomatous goiters should have surgical removal, since it is not certain as yet that x-rays will cure a large percentage of adenomas. Moreover, radiation may destroy the small amount of normal thyroid tissue which remains in some of these goiters. Whatever the treatment, however, the therapy must be guided and judged as to permanency of results by metabolic rate determinations.

EXOPHTHALMIC GOITER

In exophthalmic goiter, the metabolic rate is an important aid in the accurate diagnosis of the borderline cases, and in determining the severity of the advanced ones. Of the several typical symptoms of this disease, Judd and Plummer emphasize loss of weight and strength as the most important and when

these are present in nervous, tremulous patients, metabolism rate studies should be conducted. Exophthalmos may develop early or only after the disease has been established for several months. About 10 to 15 per cent of all cases never develop exophthalmos. Thus in deciding whether the hyperthyroidism of Graves' disease is active in a patient who is nervous, weak, underweight, inclined to perspiration, and who has an irritable heart and possible suggestive exophthalmos, the metabolic rate is obviously of greatest help. In the past three years we have seen numerous individuals with suspected hyperthyroidism and whereas the largest percentage prove to be people suffering with psychoneuroses or irritable hearts, a definite number are diagnosed as hyperthyroid and treatment has been begun in the early stages of the disease. In marked cases of exophthalmic goiter, the metabolism level is certainly the most accurate guide in indicating the severity of the intoxication. A recent instance of recurrence of symptoms two years after an extensive thyroidectomy yielded a rate of plus 80 per cent. From my clinical analysis of this case, I should have expected a rate of from plus 50 per cent to plus 60 per cent. The higher result cautions us to be very careful in advising either surgery or x-rays.

As an indication of the progress and success of medical treatment of Graves' disease, metabolic rate determinations are most important. With rest, bromides, quinine hydrobromate, overfeeding, and eradication of focal infections, the milder cases of exophthalmic goiter are often controlled and cured. Eradication of infection is especially important, and in our experience, some focus of infection in teeth, tonsils, or, as in one severe case, in the gall bladder, can usually be found. As treatment progresses, we have in the metabolic rate a means of estimating the degree and rapidity of improvement and determinations should be repeated at intervals over a period of a year or more after treatment has stopped, because of the well known tendency in exophthalmic goiter to exacerbations. The following case illustrates this value of metabolic rate studies in both the original diagnosis, the determination of the severity of the toxemia, and in the control of the medical treatment.

G. S., a girl of 17, has been nervous, tremulous, and short of breath for the past year. During the last few months she has had palpitation and tachycardia. Her eyes are naturally prominent, but

for a few months they have been especially so. Her thyroid has enlarged during the past few months. Examination showed a very nervous, restless girl, with definite exophthalmos and moderately positive eye signs of Graves' disease. She had definite fine tremor in the extended fingers, a moderate symmetrical enlargement of the thyroid, and a pulse rate of 120. Her metabolic rate was plus 26.9%. She had lost about 5 pounds in weight. She was put under medical treatment and her symptoms gradually disappeared in the course of about 4 months. Her pulse is usually normal now and her metabolic rate is within normal limits. Her naturally prominent eyes are still suggestive of hyperthyroidism, but our normal metabolic rate reassures us on that question.

Surgeons recognize in the metabolic rate a guide for surgical interference in Graves' disease. Pemberton, for instance, recently chose loss of strength, loss of weight, and the metabolic rate as the most important criteria of the operability of patients. In general, it is felt safe to operate if the metabolic rate is below plus 50 per cent, providing the heart is not decompensated and the clinical symptoms are in agreement with the rate. If the rate is over 50 per cent, ligation may be advisable, though some surgeons feel that medical treatment is as effective as ligation in reducing the metabolic rate. It is especially important that surgery is not done on a patient who has a rising metabolic rate and who is threatened with a thyroid crisis. After surgery, the metabolic rate again tells us if enough thyroid has been removed. Thus, in a recent case, a rate of plus 30 per cent persisted after operation and x-ray treatment was used to reduce the activity of the remaining thyroid tissue until the rate was within normal limits. Since these cases of incomplete relief after surgery are subject to exacerbations of symptoms with consequent danger to life, it is most important to do postoperative metabolic tests at intervals for a year or more in order to prevent any long-standing intoxication of this type.

The importance of controlling x-ray treatment by metabolic rate determinations should be more generally recognized. Whether x-ray therapy in doses usually given in itself can produce hypothyroidism or whether those cases which develop hypothyroidism during or soon after x-ray treatment would do so anyway is not certain. That the hyperthyroidism of exophthalmic goiter often is followed by a destruction of thyroid tissue with consequent hypothyroidism, however, is a well known fact, and Holmes feels that these cases of hypothyroidism which occur

after x-ray treatment belong to this group. Notwithstanding this uncertainty, it is not wise to treat a goiter after the rate is normal or when it is fast falling to normal, and no one can judge the level of thyroid secretion as well, clinically, as he can by determining the metabolic rate. A recent case which had definite exophthalmic goiter one year previously was still being treated with x-rays in spite of certain symptoms of hypothyroidism and a metabolic rate of minus 21 per cent. Thus roentgenologists should radiate thyroids only when the therapy is being controlled by metabolism studies.

X-rays, moreover, should never be administered when a crisis is approaching, as shown by a progressive increase in the metabolic rate and in symptoms, or when the rate remains stationary at a high level of plus 80 per cent or more. We feel that medical treatment should be carried out with the attempt to lower the rate or carry the patient through the crisis before radiation is begun. In 1920 and 1921 we had four cases which developed acute mania of the most severe type under medical treatment and x-ray therapy. Three of these patients died and we feel that the x-rays had a definitely bad influence on the hyperthyroidism of all. A similar experience has recently been reported by Palmer, and roentgenologists should be warned against giving x-rays when crises are impending or the metabolic rate is over 70 per cent and on the upward trend.

Between courses of x-ray treatment, moreover, it is important to estimate the metabolic rate in order to ascertain the progress of the disease. The rate usually begins to fall in from one to four months of x-ray therapy and after that period, if no reduction in the rate occurs, it is advisable to consider surgery.

It must be remembered that after either medical, surgical, or x-ray treatment has been successful, certain residual symptoms such as nervousness, tremor, irritability of the sympathetic nervous system, and exophthalmos are apt to remain. This is the result of permanent changes in the vital organs and nervous system which so often result from exophthalmic goiter. Normal metabolic rate values will show that these symptoms are residual ones rather than those of an active intoxication.

HYPOTHYROIDISM

Hypothyroidism has been diagnosed and treated, since the introduction of the metabolism test, with as great an accuracy as

has hyperthyroidism. Much uncertainty exists among the general medical practitioners in the diagnosis and recognition of mild, or even advanced, hypothyroidism, and a test which gives us a numerical expression of such secretory activity is of the greatest help. Through metabolic rate studies, Plummer has investigated the action of thyroxin, which Kendall isolated and synthesized as the active principle of the thyroid gland. He has shown, among other things, that about 14 mg. of thyroxin exists in the tissues of the normal body exclusive of the thyroid gland, that about 0.75 to 1.0 mg. of thyroxin is used by the body daily, and that a dose of about 22 mg. intravenously will raise the metabolism of a complete case of myxedema to normal. Thus, by means of these metabolic rate investigations, the diagnosis and treatment of hypothyroidism has been placed on a high plane of efficiency.

Early and mild cases of this disturbance are best diagnosed by even slightly low metabolic rates, providing the results are checked by tests done on different days. Edema, which is one of the typical signs of this disease, Plummer states, does not appear until the rate is lower than minus 15 to minus 17 per cent, and this edema may fluctuate according to the degree of strain under which the patient is placed. Gain of weight is also assumed to be a feature of hypothyroidism and yet, as we shall show below, it may not occur, although the metabolic rate is definitely low. However, it is most important to realize that all low metabolic rates are not due to a destruction of the thyroid gland. Careful clinical analysis must decide as to the cause of a verified rate of minus 10 to minus 20 per cent. Primary hypothyroidism, which produces the well known picture of myxedema, does not produce edema until the metabolic rate is between minus 15 and minus 20 per cent, and Plummer feels that a diagnosis of this disease is uncertain if edema is not present, especially when the rate is lower than minus 20 per cent. With low metabolic rates where the typical symptoms of myxedema are entirely absent, other conditions which lower metabolic rates, such as inanition, or pituitary disease, must be considered.

In this latter group, characterized by a low metabolic rate, it is probably justifiable to try thyroid therapy, and if subjective benefit comes with an elevation of the rate to the normal level, thyroid should be continued. Thyroid therapy should be

controlled by metabolic rate determinations to be sure that too much is not being given, or to see that the patient is actually absorbing it from his intestinal tract. Plummer emphasizes the fact that certain cases with diffuse colloid goiter or patients having a low metabolic rate not attributable to thyroid gland destruction, are often unable to absorb desiccated thyroid, and more often thyroxin itself, from the intestinal tract even when given in massive doses. This non-absorption of thyroid, when given by mouth, explains the evident lack of benefit which at times is apparent with thyroid therapy.

Thyroid therapy finds in the metabolic rate, therefore, a definite guide as to the necessity of administration, as well as the amount, which should be given. It has been considered justifiable to give thyroid in 5, 10 or 15 grain doses to obese individuals for reducing purposes, on the assumption that thyroid is lacking. Yet Means pointed out several years ago that very few obese patients are hypothyroid as determined by metabolic rate studies, and we have come to the same conclusion in our work. The administration of thyroid to normal individuals is pernicious, since an artificial hyperthyroidism is often established, and definite damage to the nervous system and vital organs is thus produced. One individual, seen five years ago, after taking large doses of thyroid for about two months, had acute dilatation and permanent fibrillation of the heart. We feel, however, that it is justifiable to treat any individual with thyroid who exhibits symptoms suggestive of a deficiency of this secretion, and whose metabolic rate, after several accurate tests, falls constantly below minus 10 per cent. We have found that cases with rates between minus 10 and minus 20 per cent usually require 1 to 2 grains of desiccated thyroid daily, and that those with rates between 30 per cent and 45 per cent require from 3 to 6 grains daily to keep the metabolic rate normal and relieve their symptoms. These doses are the same as those recommended by Means, Janney, and Plummer. It is thus seen that the usual doses suggested in our text books are too large and are apt to work harm to the patient.

The difficulty of being sure of the diagnosis of hypothyroidism from the clinical point of view accounts for the confusion which exists in the medical mind in regard to this disease. Many cases of myxedema are being treated for Bright's

disease or myocardial insufficiency, because of the subcutaneous swelling and general pallor which exists. And because of the relative rarity of advanced cases of myxedema, the medical man does not become aware of the fact that a marked secondary anemia arises in these patients, and the diagnosis of nephritis is made, in spite of the solid edema, the dry skin, the low temperature, the loss of hair, and the listless mental state that exists. We have seen two such cases recently, and both have been completely relieved by thyroid therapy. In the diagnosis of these cases the metabolic rate is of the greatest importance.

And in the diagnosis of the early stages of severe hypothyroidism before much swelling, anemia, loss of hair, and even much mental torpor exists, the metabolic rate is a great help to the physician. The following case is an example of the early diagnosis of myxedema, made possible largely through the test we are considering.

J. S., a married woman, aged 27, was referred with the diagnosis of possible hyperthyroidism. She has been slightly nervous, has had a moderate goiter for 5 years, and for the past year her eyes have been slightly prominent. On being questioned she gave the history of marked coldness of the body, especially during the last three months, drowsiness during the preceding month, a marked loss of energy and enthusiasm, and a loss of weight from 120 to 107 pounds. Physical examination showed that she was under weight, had a slow mental reaction, a slight drawling in her speech and slight facial edema. She had exophthalmos without other eye signs of exophthalmic goiter, and a soft symmetrical goiter of moderate size. Her pulse rate was 75. There was a slight indefinite tremor. The metabolic rate was minus 28% at the first reading and minus 37% at the second test a week later. This difference may be accounted for by the possible influence of her menstrual period, and by the newness of the procedure at the first examination.

The above history is an instance of an early case of myxedema diagnosed definitely through the aid of metabolism studies. This woman had only slight facial edema and had lost instead of gained weight. She had no anemia, and only lately had noticed loss of strength and mental agility. She is an example of the group of small and large goiters which are associated with hypothyroidism.

The following case is an instance of hypothyroidism being the cause of unusual symptoms in the absence of the typical picture of the disease:

K. M., a woman, aged 50, single, complained of severe headaches, and rheumatism in her shoulders and knees. Her headaches had been present for two years and of late they had been continuous, especially through the frontal region. During the first year she had nausea and vomiting with the severe headaches. She had gradually been weakened by these headaches and consequent loss of sleep and she had become so nervous and depressed that she was unable to do her work. A careful physical examination, including x-ray investigation of sinuses, cranium, and gastro-intestinal tract, together with a Wassermann test, blood count, and stomach analysis, was done in my office. This routine had already been carried out by two other physicians. As before, the findings were negative. On account of coldness of the body, thin eyebrows and hair, suggestive edema, her metabolic rate was determined and found to be minus 20%. She was given thyroid, and though I thought her headaches and rheumatism were due to some cause as yet undiscovered, she has become entirely relieved of all her symptoms and has remained so for several months.

It is thus seen that by using the routine metabolic test on all individuals who suggest the possibility of hypothyroidism, many early, as well as advanced, cases of this disease will be diagnosed with a certainty impossible before the advent of this method of investigation.

CONCLUSION

After the constant use of basal metabolic rate determinations for a period of over three years, we are convinced of their value in the diagnosis and treatment of both hyperthyroid and hypothyroid states. The borderline cases especially can be diagnosed, and the etiology arrived at, far earlier than would be possible without its aid. As a guide for medical, surgical, or x-ray treatment in hyperthyroidism, the metabolic rate is indispensable. As a means of determining the advisability of thyroid treatment in cases of obesity and in hypothyroid states as well as regulating the amount of thyroid given, indirect calorimetry has given us an invaluable guide. Finally, in investigation, it already has yielded much information about thyroid secretion and disease which is of great aid to the medical profession.

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EXPERIMENTS ON THE ENDOCRINOLOGY OF THE SEXUAL GLANDS

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The internal secretion of the sexual glands occupies a most important position within the science of endocrinology. The reason for this is due, not alone to its biological importance in general, which has always made it a subject for deep study, but especially to the fact that in the last decades the experimental work of a number of scientists all over the world, as for instance: Ancel and Bouin, Athias, Champy, Goodale, Harms, Lillie, Lipschütz, Meisenheimer, Pézard, Sand, Steinach, Tandler and Grosz and others, has advanced our knowledge considerably, has given new scientists the desire to continue their studies, so that the literature of the past few years is steadily on the increase and already approaches the point where it cannot be grasped.

I will not on this occasion broach this subject, but, in accordance with the editor's wishes, confine myself to a short, connected account of my own experiments in this field.

I myself have worked on these problems since 1914. My earlier experiments were published partly as a Danish monograph and partly scattered in different treatises, especially French and German.*

I can now supplement the older experiments with new results. In my account attention will be paid particularly to the essentially endocrine side of the problems. The histological problems, which are certainly of great interest and which at present, through a wrong tendency, are about to overshadow the

*Sand, Knud: Experimental studies on the sexual characters of mammals (Danish). Copenhagen, 1918, 256 p., 42 illustr.

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much more important endocrine aspects, have been intimately treated by me before, and hence will be only briefly mentioned. Spatial limitations also necessitate my confining myself to my own experiments.

My experiments, which for the most part were made in 1914-17 at the *Institute for medical jurisprudence* at the *University of Copenhagen* and later continued at the *Institute of Pathology* in the *Municipal Hospital of Copenhagen*, have had the study of the endocrinology of the sexual glands as their chief subject.

The main object I had in view was to examine the specificity of the sexual hormones and their influence on the homological and heterological organism, thereby to determine the question of the sex-transformation, and finally the question of the locality where the sexual hormones are produced in the gonads, which tissues are "sexual hormone tissues."

By the study of these problems it had been possible, as before, to confine oneself to working only with a *single effect* either with *male* or with *female* hormones on the experimental animals and thus only examine *non-combined* sexual characters. But in order also to analyze *combined* sexual characters, in 1914 I began to make experiments of *combined hormones*, i. e.: both male and female simultaneously on the same organism. In this way I wished to examine whether or not there was an "antagonism" between the gonads and the sexual hormones, as presumed by Herbst and Steinach, or perhaps only a certain obstacle, a certain immunity in the organism against the heterological gonad, and finally it was my intention, by means of an eventual production of experimental hermaphroditism, to find a possible explanation of hermaphroditic and other abnormal sexual conditions.

Thus it can be seen that, on a broad experimental basis, I took up for examination as a whole, most of the problems belonging to the endocrinology of the sexual glands.

My experimental animals have been rabbits, guinea-pigs, rats and dogs. Further, several operations were made on human beings.

In order to convey an idea of the experiments made, the following table is given here:

I. Experiments on the effect of non-combined hormones, throwing light upon non-combined sexual characters.

A. Experiments throwing light upon male sexual characters.*

1. Testis Transplantations:

a. Autotransplantations

One stage operation.

Two stage operation.

b. Simultaneous auto- and iso-transplantations on the same male.

c. Isotransplantations

Homological (from male to male).

Heterological (from male to female).

2. Other experiments throwing light upon male sexual characters:

a. Operations on vas deferens.

b. Experimental cryptorchism.

B. Experiments throwing light upon female sexual characters.

Ovary Transplantations:

a. Autotransplantations.

b. Simultaneous auto- and iso-transplantations on the same female.

c. Isotransplantations.

Homological (from female to female).

Heterological (from female to male).

II. Experiments on the effect of combined hormones throwing light upon combined sexual characters (experimental hermaphroditism).

Just as I took up as many series of experiments as possible, so also has my *technique*, described elsewhere, been varied in many ways. For example, I introduced puncturing of the transplants, which clearly produced better conditions for the invasion of the vessels; in transplantation of the testis in two stages I made a primary sewing on the wall of the peritoneum, a method (also used by Steinach) which gave excellent results. I alternated with consanguinity and non-consanguinity, in many ways varying the places of transplantation and in a simple manner by

*Nomenclature: *Isotransplantation* (Homolotransplantation) means transplantation from one animal to another of the same species; *Homological*, between two animals of the same sex; *Heterological*, between two animals of different sex; *Allotransplantation*, between two animals of different species (rat-rabbit); here, too, the adjectives homological or heterological can be added, referring to sex. This nomenclature is simple and is always practical when used.

simultaneous auto- and iso-transplantations showed better results of the autotransplantations. Want of space prevents me, however, from going into details regarding the approximately 700 experimental animals (the most important tables are to be found in my Danish monograph), but I will give a summary account of the most important results.

PHYSIOLOGICAL RESULTS

All of the results have confirmed in every detail the theory of the internal secretion of the sexual glands and given striking evidence of the hegemony of these in the governing of sexual character conditions without, of course, excluding other endocrine glands taking part in the development of the phenomena.

In my report I will follow in principle the table given above. Unless otherwise mentioned, the experiments date from 1914-17; later experiments will be inserted in their respective places, especially under vas deferens operations, as regeneration experiments and under experimental hermaphroditism.

I. Experiments on the effect of single, male or female, hormone (These comprise all of those experiments described under I, A and B.

1. Testis Transplantations

By more than 50 experiments, distributed through the above-mentioned groups, and performed with differing technique, I have confirmed the previously scarce positive reports to be

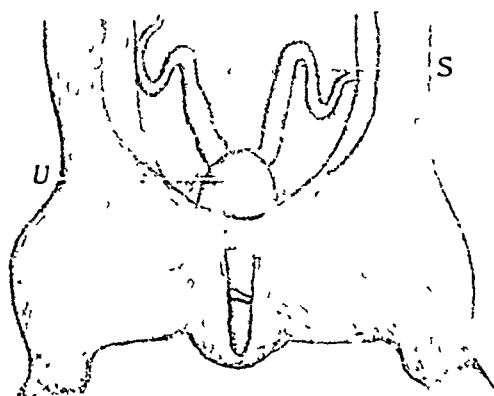


Fig. 1
Guinea-pig No. 140. Positive homological isotransplantation of testis with normal development of all characters.
S: glandulae vesicales.
U: urinary bladder.

found on testis transplantation, the best of which, as known, being Steinach's autotransplantation and heterological isotransplantation ("masculinization"), and showed the possibility of the experiments under new conditions, such as simultaneous auto-

and iso-transplantation on the same animal, and homological iso-transplantation, which hitherto had not given positive results. As an illustration of this is given Figs. 1-3 of positive homological isotransplantation with castrated control animal and a microscopic picture of the transplant.

Fig. 2

Guinea-pig No. 141. Typical castrate - sexual - characters in control animal.

S: glandulae vesicales empty and atrophic.

U: urinary bladder

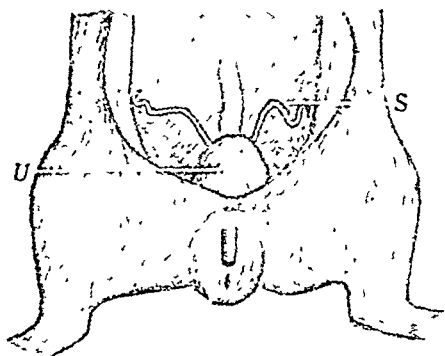


Fig. 3

Section (for Fig. 1) of the testis transplant (fixation: liquor Flemming). Between four atrophic canals (a), containing only partly degenerate Sertoli cells (b) and an amorphous mass can be seen the enormously augmented groups of normal, plentifully granulated Leydig cells (c), often imbedded around vessels (d).

As a microscopic illustration of the autotransplant at two stages, Fig. 4 is given, a new example of the most frequently found conditions in testis transplants.

Even though the things explained in these illustrations are the most frequently found, quite other conditions can be found in some cases. Fig. 5 shows a microphotograph of a transplant from a rat, in which the Leydig cells were scarce, without the usual hypertrophy, while there were several unusually well de-

Fig. 4

Guinea-pig No. 94. Testis autotransplant at two stages. Four atrophic canals with thickened membrana propria, containing partly degenerate Sertoli cells and an amorphous, thready substance. In between the canals strongly augmented Leydig cells with plentiful osmic stained granules



Fig 5

Rat No 150. Homologous isograft of testis with nearly negative result. Transverse section of transplant. In the center necrosis; the nearer it comes to the periphery the better are the canals preserved, and best at the edges (as indicated by line), where they contain epithelium which lacks only spermatozoa. The canals are surrounded by touches of connective tissue in which only a few Leydig cells were found here and there.

veloped canals with Sertoli cells, spermatogonia and spermatocytes. But in this case, which differed from the others, the hormone effect was very weak, the penis attaining only one-third of the normal size, glandulae vesicales were atrophic and the male tendency psychosexually was weak.

Special attention attaches to my heterological isotransplantation of testicles, which were a confirmation of Steinach's masculinization experiments, at that time only briefly made known.

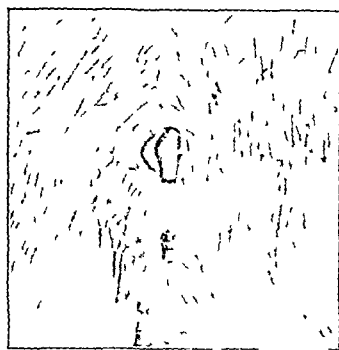
I particularly wished to examine whether it was impossible by testis transplantation in castrated females to produce hypertrophy of the clitoris, homologous to a penis, a problem to which Steinach, strange to say, had not paid special attention. In 1916 for the first time Lipschütz made known that he had observed this phenomenon in one of Steinach's guinea-pigs

Fig 6

The drawings show the surrounding part of genitalia externa in a masculinized female castrate and in control animals



A Female castrate



B Masculinized female castrate.

A Conditions in female castrate the bisected fold in the skin, covering the rudimentary clitoris, which cannot be brought out of the folds

B. Conditions in a female castrate masculinized by heterological testis isotransplantation. Out from the folds of skin, which are turned back, the strongly hypertrophied clitoris protrudes, presenting itself as a small penis ("peniculus"). See Fig 6-D

In a number of castrated female rats I succeeded in producing, besides an astonishing inversion of the psychosexual character, different degrees of clitoris-hypertrophy, "peniculus." This strikingly demonstrative somatic sign of sexual transformation showed an exact reaction on the male hormones, a reaction which could be compared exactly with mamma hypertrophy in the feminized male animal. The phenomenon is explained by the text illustrations.

As is well known, attempts have been made in recent years to profit from the experience gained through testis transplantations on animals by applying the method with different objects in view to human beings (in treating the results of castration, senility, etc.).

C Normal male

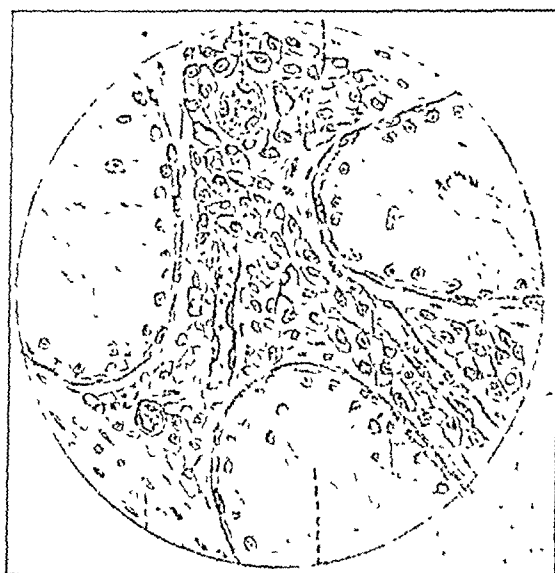
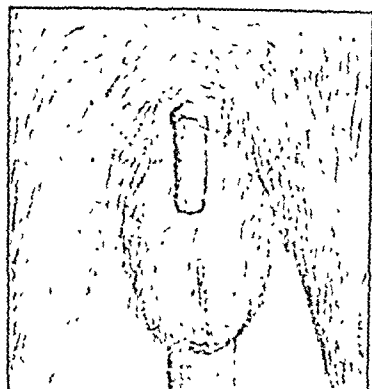


FIG. 6-D
Microscopic conditions in transplant from rat No. 224, masculinized (Fig. 6-B). Atrophic canal with a few scattered cells, strongly augmented Leydig cells and blood-vessel (indicated by dotted lines).

As some of the first I will only give the reports of Lepinasse and of Lydston. Special interest was awakened by Steinach's and Lichtenstern's accounts (1918) of testis transplantation with positive results in castrated homosexuals, later followed by more cases (Mühsam).

At present I will only say that, in 1921, in the 5th ward of the City Hospital of Copenhagen, I performed at the patient's earnest request two operations of this kind, using by way of experiment one-sided castration with subsequent testis transplantation. The cases in question were two congenital homosexual persons about 28 years old, both suffering keenly on account of their condition. In one case the material was unsatisfactory, coming from an older man with hydrocele; in the other case, from a young man with cryptorchism. Neither of cases has as yet, after about a year's time, shown indubitable results; the transplants seem to have been resorbed.

2. *Other Experiments Throwing Light Upon Male Sexual Characters*

Operations on the *vas deferens* (Under this head so-called *regeneration experiments*).

The most important experiments hitherto on this subject were those of Bouin and Ancel (1903-04), by which they established the theory of "la glande interstitielle," the Leydig cells as carriers of the internal secretion of the testicles.*

My series of experiments were the following:

- (a) Resectio vasis deferentis unilateralis.
- (b) Resectio vasis deferentis bilateralis.
- (c) Resectio vasis deferentis unilateralis, combined with castratio contralateralis.
- (d) Transcisio vasis deferentis unilateralis, combined eventually with contralateral castration or resection.

A *résumé* of this series of experiments follows.

Resection of the *vas deferens* proved to be an operation as a rule slowly affecting the testis structure. It should always be made on grown animals, as it does not begin to take effect until after puberty, doubtless through the spermastasis, then successively developed. But even after puberty the experiments seem to turn out rather whimsically; often at least six months must pass, more often a longer time, before any clear result can be traced; sometimes even a year does not seem long enough. My method

*It is this tissue which Steinach later named, not very aptly, "Pubertaetsdrüse," and which at the present under the name "Pubertaetsdrüsenlehre" is the subject of not so little, but misunderstood criticism in the German press; the doctrine is actually due to Bouin and Ancel. My personal experiments on these subjects (see especially J. de physiol. et de path. gén., 1921) have been misunderstood and wrongly reviewed, especially by two German authors (Stieve, 1921, and Harms, 1922).

for "experimental cryptorchism," described below, has proved to be quicker and surer for studying Leydig cells.

The foregoing is also true as regards the results of trans-cision, the simple cutting through of vas deferens, which in my experiments appeared to act as a resection, it being impossible to keep the vas deferens open intra-abdominally.

By unilateral resection combined with contralateral castration, I have confirmed Bouin and Ancel's discovery: Together with a strong atrophy of the generative tissue an enormous hypertrophy of the Leydig cells was found, possibly a compensatory hypertrophy. In testes of this kind I was not able to show to a certainty regeneration phenomena in the canals; the atrophy approached, on the contrary, the extreme.

The sexual characters developed normally in all the experiments; it was of special interest that I also in experiments with resectio unilaterialis combined with castratio contralateralis, found not only the physical characters fully normal, but the libido was even unusually powerful.

The different discoveries spoke greatly in favor of ascribing the most important production of the male sexual hormones to the Leydig cells.

In many cases I found, as did Tournade, that after resection a "spermaecyste" developed below the distal ligature, a phenomenon which, by relieving the sperm secretion, probably retards the result from going into effect.

My results from vas deferens experiments coincided therefore with those of Bouin and Ancel and of Tandler and Grosz.

There is, however, no doubt but that this field of experiments is very difficult and the conditions complicated, which has once more been shown by recent experiments, partly coinciding with the above-mentioned authors (as for example by Kuntz) and others disagreeing with them (as for example by Tiedje). They are not, however, in any way convincing, and it is best to keep to Bouin and Ancel's theory, which was arrived at through lucid experiments.

As is known vas deferens experiments have recently obtained a renaissance through Steinach's employment of them for the purpose of so-called rejuvenation, or rather regeneration or restitution, on old animals.

In this field I have at present some experiments under way which are expected to throw light upon the question in inverted order, namely, to determine whether animals on which vasoliga-

tion or experimental cryptorchism has been performed when young, have a longer life than their normal brothers.

These experiments I shall reserve for later publication. I will give here only a single regeneration experiment with a very successful result, on a hunting dog (for details see *Compt. rend. de la Soc. de biol.*, 1921).

In May, 1921, a pedigreed German pointer, 12½ years old, whose life the owner despaired of, owing to senile changes, was brought to me. He contemplated having the dog killed. I took the precaution of sending the animal to Prof. Hansen of the Royal Veterinary College for a preliminary report. This affirmed that the dog suffered from pronounced senility, with the symptoms of dull eyes, thin coat, deafness, and thickened, inelastic skin. It could move only with difficulty, was emaciated and often had incontinence of urine and feces; there were no signs of organic disease except a slight albuminuria, which is so frequent in old dogs; a tuberculin test proved negative. In spite

Before the operation.



Fig 7

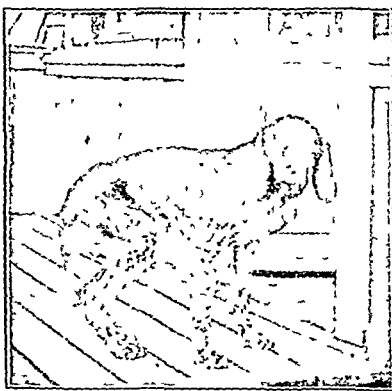


Fig. 8

of misgivings as to whether an anaesthetic would be borne, I performed, on May 23, resection of the left epididymis and right-sided vasectomy. At the end of June the animal was returned to his owner, who, on Oct. 25, wrote that three or four weeks after his discharge the dog became brisker, its appetite better and its coat thicker. By the end of August it could run behind a bicycle ridden slowly, and the sexual appetite revived; sight improved and it no longer slept all day. In September great strides were made, so that the owner again used it for sporting purposes and regarded it as equal in every way to a dog seven years old. The animal was again examined by the veterinary authority, who expressed great surprise at the change in it. (See Figs. 7-10).

In spite of its precarious condition at the time of operation, the dog lived for more than a year after. It died June 12, 1922, during a stay in the country, unfortunately at a time when the author was on a lecturing tour in Paris. This unfortunate coincidence is the reason why a dissection was not made in spite of all instructions. The owner has written the following about the last half year: "The good condition continued and improved further in the winter of 1921-22; for example, with respect to mobility and endurance. From April, 1922,

After the operation.



Fig. 9



Fig. 10

the recovery began to cease; digestion especially was always in disorder. On June 10, it had a bad attack of diarrhoea, accompanied by coughing and difficulty of breathing and died rather suddenly on June 12 before I could get hold of a veterinary surgeon." The whole progress of the disease resembled an acute intestinal poisoning. Unfortunately the lacking dissection precludes the possibility of a critical judgment of the case; it is of interest, however, on account of its well observed clinical progress and should greatly encourage new experi-

ments. A restitution period of one year, as stated, for a dying animal whose normal age reaches 12-13 years is a valuable result; a dog's year is reckoned as equal to 7 human years.

With respect to *regeneration operations* by means of vasoligation on *human beings*, this is a problem which, at present, after the publication of Steinach, 1920, is being dealt with all over the world.* I, myself, began them in September, 1920, and recently published my first 15 cases in "Ugeskrift for Laeger," June, 1922 (English translation will appear in *Acta chirurgica scandinavica*). I will only mention that several of them show such positive results that the conclusions can hardly be disputed, and that these greatly encourage further investigation.

II. *Experimental Cryptorchism*

While earlier investigators of the study of sexual characters and hormones in cryptorchid animals (especially Bouin and Ancel) have looked for their material mainly in cryptorchism occurring in nature, I pursued another course, supplying myself with constant material by producing experimental cryptorchism. The technique was extremely simple in that I pushed the testes up into the abdomen and by a small laparotomy closed the inguinal canals. The artificial cryptorchidic testis then lies free in the abdomen, just as in the case of a natural abdominal cryptorchism.

The experiments come under the following groups:

- (1) Oclusio canalis inguinalis bilateralis.
- (2) Oclusio canalis inguinalis unilateralis.
- (3) Oclusio canalis inguinalis unilateralis, combined with resectio vasis def. contralateralis.
- (4) Oclusio canalis inguinalis unilateralis, combined with castratio contralateralis.

Just as in experiments with vasoligation the testes were measured and weighed during dissection. Microscopy took place after fixation in Flemming's liquid.

A *résumé* of results in the 4 groups follows.

It was discovered that in experimental cryptorchism (abdominal) executed by oclusio canalis inguinalis, there can be produced macro- and micro-scopic changes of the inclosed testes of the same kind as we find them in natural cryptorchism. An inclosed testis was quickly reduced in size, sometimes after 3

*For literature see: Harms, *Fortschr. f. naturwiss. Forschung* xl., 5, 1922; and P. Schmidt: *Theorie und Praxis d. Steinachschen operation*. Wien., 1922.

months, to one-third and after a longer time to one-tenth of the weight of the contralateral, normal testis.

It turned out that this experimental technique was much quicker and more certain in its effect than the vasoligation, in experiments on the question of the hormone tissues of the testis.

The existing atrophy of the spermatic canals was accompanied by a certain slighter or stronger hypertrophy of Leydig cells; this was most pronounced after occlusion in full-grown animals; less after occlusion in infantile animals, and seemed, besides, to increase with the duration of the occlusions and degree of canal atrophy. Fig. 11 is given as an example.

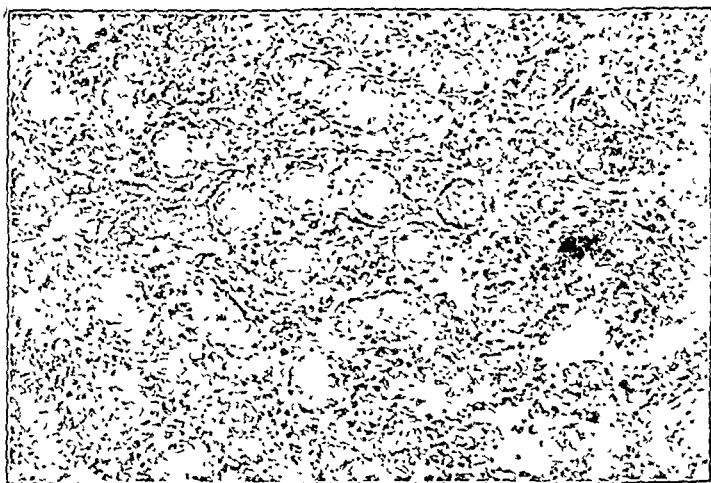


Fig. 11

Guinea-pig No. 124. "Experimental cryptorchism," produced on an infantile animal by an 11 months' bilateral occlusion of the inguinal canal. Microscopic photograph shows a general view of testis: the strongly atrophic canals, surrounded by enormously augmented Leydig cells. Fig. 12 of normal guinea-pig testis, magnified to the same degree, will serve for comparison.

I have succeeded experimentally (through one-sided occlusion of the *canalis inguinalis* combined with contralateral castration) in 3 cases in producing phenomena which can be interpreted as a compensatory hypertrophy which, judged from everything, is due alone to the Leydig cells.

All of the groups of experiments corroborate, to the greatest extent, the theory that the Leydig cells are substantially the most important for production of the male sexual hormones. These older experiments from 1914 to 1917 I have taken up later. A single preliminary result of the new experiments I shall merely

mention on account of its interest for the question of an eventual transformation of connective tissue cells to Leydig cells.

In some of the experiments on rats, which were examined as early as three months afterwards, the inclosed testes were found reduced to one-third of the weight of a normal control animal's testes. The microscope showed—besides an advanced atrophy of the canals and a very considerable hypertrophy of the Leydig cells—a new phenomenon which, most probably,

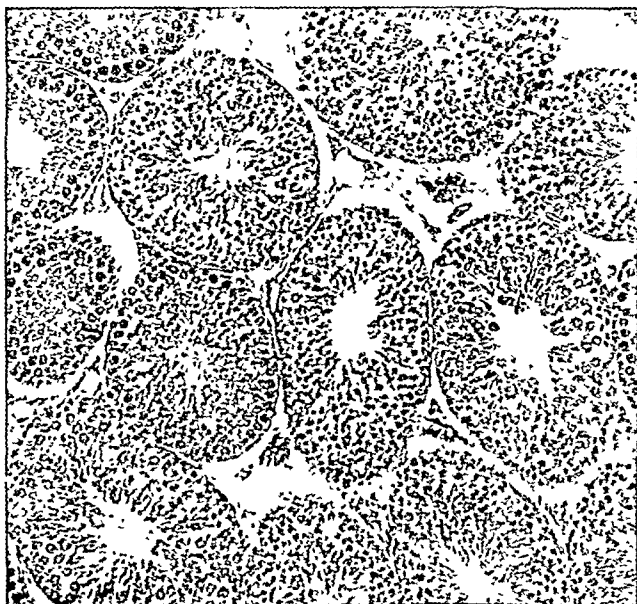


Fig 12

Microphotograph of normal testis from a pubescent guinea-pig. Between the canals quite small groups of Leydig cells can be seen.

escaped attention in the older experiments on account of the treatment being with osmium (in the experiments dealt with here formalin fixation and coloring by hematoxyline-eosine were used). In the intertubular tissue there were found, scattered among the ordinary connective tissue cells and the large groups of Leydig cells (most often in between these) typical eosinophile cells, so numerous and constant that the phenomenon could not be caused by chance. Although at present I cannot explain this peculiar phenomenon, I am inclined to think that these cells possibly represent a passing (transient) stage during a trans-

formation of connective tissue cells to Leydig cells, especially in the case where these are greatly augmented.

III. Experiments throwing light upon female sexual characters.
Ovary Transplantations

I performed a considerable number (167) of these in 1914-17, arranging them under the above-mentioned groups, which contain all possible types. All of the experiments corroborated the theories of the endocrine function of the ovaries with regard to the sexual characters, in auto- as well as in iso-transplantations. By heterological isotransplantations I verified Steinach's feminization experiments. An ovary transplanting from a posi-

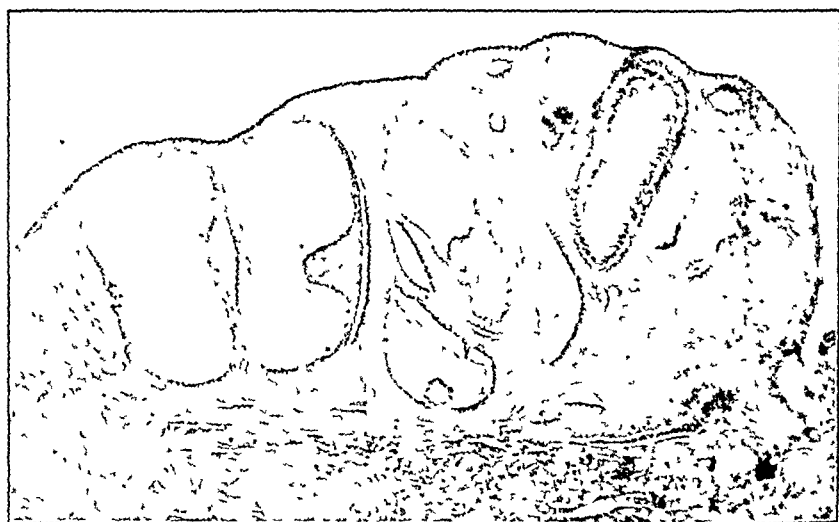


Fig 13

Guinea pig No 37. Positive heterological transplantation of the ovary ("feminization"). Microphotograph. In the transplant are found follicles and theca lutein tissue, but no corpora lutea.

tive feminization in a guinea-pig can be seen in Fig. 13, which shows how nicely a transplanted ovary can preserve itself in the castrated male organism.

In all the series of ovary transplantations altogether 167 transplants were used. As opposed to earlier scientists I examined these in serial sections, in order to substantiate the appearance of the three elements (follicles, theca lutein tissue and corpora lutea), and thereby be able to determine the question of the place of production of the female sexual hormones.

Résumé of the results of ovary transplantation:

The place of transplantation and the consanguinity of the donor and the host seemed to be factors of slight importance for the result.

Autotransplantations were successful, on guinea-pigs especially, easier than homological isotransplantations, and these again easier than heterological.

The principle that the ovary by internal secretion has a specific developing influence on the accidental female sexual char-



Fig 14
Guinea pig No 37
'Feminization'. Micro-
photograph shows (com-
pare Fig 15) the
strongly hypertrophic
papillae mammae. In
the tissue under this
the sparingly scattered,
empty alveoli

acters has again been confirmed by my series of ovary transplants.

By heterologous isotransplantations, confirmation of Steinach's feminization was found

The anatomical conditions of the transplants showed that it is possible to get only a relative isolation of the ovary elements by a more or less complete elimination of one or two of these elements. Most frequently all three were found; as a rule corpora lutea dominated the picture together with often

only insignificant quantities of the other tissues; the least resistant were the follicles.

The heterological isotransplants partly showed a remnant, most frequently not well preserved, and partly gave the information that the follicles in the heterological organism *can*, of course, develop into maturity but more often tend toward atresia, so that the theca lutein tissue is increased; on the other hand, maturing with subsequent corpus luteum formation, as found in

Fig 15

Microphotograph (magnified the same as Fig 14) shows papillae mammae in a normal female in puerperio. In the underlying tissue large conglomeration of glandular tissue



auto- and iso-transplants, almost the same as in normal ovaries, only very seldom takes place.

A comparison between the hormone effects in transplants, their approximate number (they were measured by *micrometry*) and their contents of the three ovarian elements showed that a small quantity of all three elements can be found without any traceable hormone effect. Quantitative laws seem to rule: in order to produce a hormone effect a certain "minimal quantity" of ovarian tissue is required. In transplantings with plentiful

ovarian tissue with normal hormone effect, widely different combinations, in quantity and kind, of the three elements were found.

On the whole the results of my experiments in 1914-17 did not indicate the production of the female sexual hormones in any single one of the ovary elements, but supported, in the highest degree, the latest views, especially in the form put forth by Bucura, according to which the three elements, morphologically and physiologically, must be seen from a common visual angle, and under different conditions can act vicariously or substitute for one another in their effect upon the female accidental characters.

I have several series of new ovary transplantation experiments under way on the interesting problem: transplantings and potentized hormone effect. Previously, in the older experiments, I found certain signs with regard to this, and my newer experiments, which will be published later, have given further support to the supposition that the ingrafted sexual glands produce a potentized hormone effect, a phenomenon which coincides with what Steinach and Holzkecht discovered after x-raying ovaries.

II. Experiments on combined hormone effect, throwing light upon combined sexual characters.

“Experimental Hermaphroditism”

In the older experiments (1914-17) I tried to solve the problem in the following ways:

1. Transplantation of heterological sexual glands into non-castrated animals.
 - A. Testis transplantations into normal infantile females.
 - B. Ovary transplantation into normal infantile males.
2. Simultaneous transplantations of homological and heterological sexual glands into the same castrated infantile animal.
 - A. Simultaneous transplantation of ovary and testis into castrated infantile female animals.
 - B. Simultaneous transplantation of testis and ovary into castrated infantile male animals.
3. Intratesticular ovary transplantations (“artificial ovario-testes”).

With regard to the first groups it appeared that it was possible, indeed, to a certain degree to get a heterological transplant to grow in a normal animal, but it was obviously more difficult than in castrated subjects, and it seemed as if there exists in normal organisms a certain hindrance for the ingrowth of heterological gonads.

The arrangement of the experiments was, however, unequal, in that the normal gonads were from the beginning given preponderance over the transplanted. I therefore went over to combined hormone experiments by simultaneous transplantation of

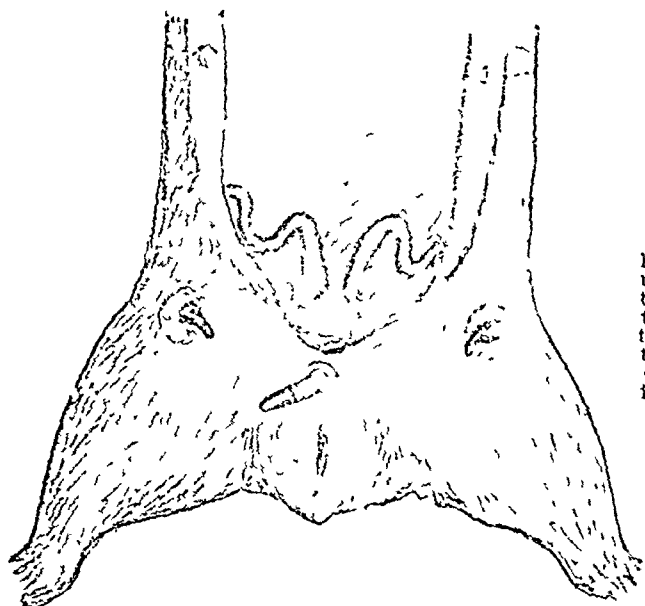


Fig 16
"Experimental
hermaphrodite," 3
months after simul-
taneous ovary and
testis transplanta-
tion. Ovary in right,
testis in left side
(near top of draw-
ing).

both kinds of gonads into the same infantile castrated animal. (Hitherto no experiments of this kind had been made. Steinach's publication on this subject came out in 1916, Arch. f. Entwicklungsmech. B. 42; but the fact that Steinach and I, independently, have reached substantially the same result in this difficult sphere, seems to me to confirm, to the highest degree, the correctness of the experiments.)

Experiments of this kind on female animals gave no particularly positive results. On the other hand, I succeeded, as did Steinach, in this way in producing experimental hermaphroditism in infantile male animals. Fig. 16 shows an animal of this type, bisexual somatically as well as psychically; the peculiar combination of penis, seminal vesicles filled with secretion,

and large, full mammae, secreting normal milk, can be seen. Psychosexually the animal was bisexual according to which animal was placed with it (male, female, young ones).

Microscopically in the well-ingrafted testes was found enormous development of Leydig cells among atrophied canals as

Fig. 17

(For comparison with Fig. 16). Normal nipples of: a, normal male (4 months old); b, normal female (4 months old); c, normal female (in puerperio).



usually in testis transplants. In the ovary numerous mature follicles and some theca lutein tissue appeared. The mammae showed an abundance of glandular tissue almost of the same type as in a puerperal mamma.



Fig. 18

(Rat No. 111). "Artificial ovariectomy." Testis tissue with spermatogenesis (I). In the ovary a tertiary follicle (F) and corpus luteum (C), and at L, Leydig cells.

Intratesticular Ovary Transplantation

This method of producing experimental hermaphroditism I took up in 1914. Through a small incision in albuginea testis the ovary is placed in the middle of the testis by a delicate pincette. No suture is used. Preliminary experiments on rats

showed that the ovary, even with comparative ease, grows into the testis itself and can develop here and form corpora lutea in a mature as well as in an infantile testis. Also it was found that a testis, inclosing an ovary, can still develop further to full spermatogenesis or preserve a spermatogenesis already developed. In short, it was found possible to preserve ovariotestes in which both gonads thrive well in the most intimate union without any reciprocal hindrance.

The actual endocrine results from experiments on guinea-pigs were the production of experimental hermaphroditism with bisexuality in somatical and psychical characters as described above. Fig. 19 shows an artificial ovariotestis of this type.

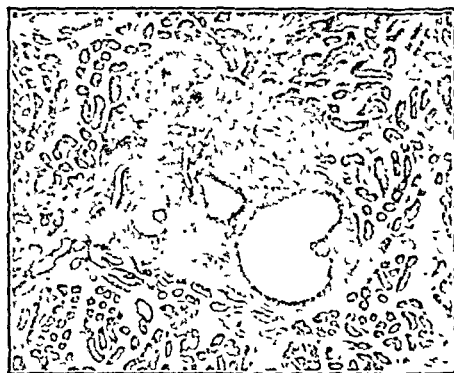


Fig. 19
"Artificial ovariotestis," producing "experimental hermaphroditism" in an infantile guinea-pig (No. 217).

Thus new evidence was secured that testis and ovary thrive well in this intimate symbiosis and develop their hormone influences independently of each other and without reciprocal hindrance by this method.

A specially interesting phenomenon is seen in the mammae of these animals; the experiments actually showed that mammary hypertrophy with secretion of milk to an extent that suggests puerperal phenomena can be produced without corpora lutea, without uterus ("glande myometriale"), and without the fruits of pregnancy—in a male organism.

On the whole, the way has been prepared for experimental work with combined hormone effects through such experimental hermaphroditism, and opens, to a certain extent, a new possibility of understanding abnormal sexual conditions and, perhaps, for the treatment of these.

With reference to the question of *antagonism** a number of my experiments also seemed to suggest a certain hindrance in the normal organism with respect to ingrowth of heterological, opposite gonads. On the other hand, my simultaneous bisexual transplantations succeeded, and my positive intratesticular ovary transplantations showed more especially that a real antagonism is out of the question.

I could more readily imagine this hindrance mentioned before, explained by a kind of "atreptical immunity" in the normal organism from the heterological sexual gland in about the following manner: In every organism are found certain substances which are necessary for the sexual glands, and these substances the latter try to absorb to the greatest possible extent. The normally situated gonads have the best chances of being able to absorb these substances, for which reason heterological (perhaps also homological) gonads transplanted into normal organisms, cannot get enough of these substances and therefore perish. Homological and heterological gonads, which have been transplanted at the same time into the same organism, are both able to grow in, having both about the same opportunity of absorbing the substances. Further, the phenomenon that ovaries ingrafted in the testes find good conditions for developing there, can probably be explained by a similar theory, in that the substances of the normal male organism, necessary for the gonads, are stored up in the testes, both kinds of gonads thus being able to make use of them.

A problem of such scope as experimental hermaphroditism is not solved, of course, by these experiments by Steinach and by myself. There are still problems enough left.

I have made more recently several *new series of experiments* regarding which the reader is referred to an excerpt from a lecture in *Compt. rend. de la Soc. de biol.*, June, 1922, and more detailed in *J. de physiol. et de path. gén.*, October, 1922.

As among the most important of the *newer results* the following may be mentioned. While earlier experiments were made

*The American author, Moore, has recently taken up hermaphroditic experiments on rats. In these he has confirmed the phenomenon, well known from a series of older authors (c. g., Schultz, Foa, Katsch, Basso, Sand) that heterological glands can be made to grow in normal animals. My standpoint with regard to antagonism he seems not to have understood. Perhaps I have not expressed myself quite clearly in the very brief English excerpt in *J. Physiol.*, 1919. I beg to refer further to Bohn's criticism of Moore's experiments (in *Revue scientifique*, Nov. 6, 1921).

on infantile animals, I have now succeeded in producing the hermaphroditic phenomena in two months' old animals, therefore just at the time of puberty, and even in animals towards



Fig. 20. Experimental hermaphrodite.

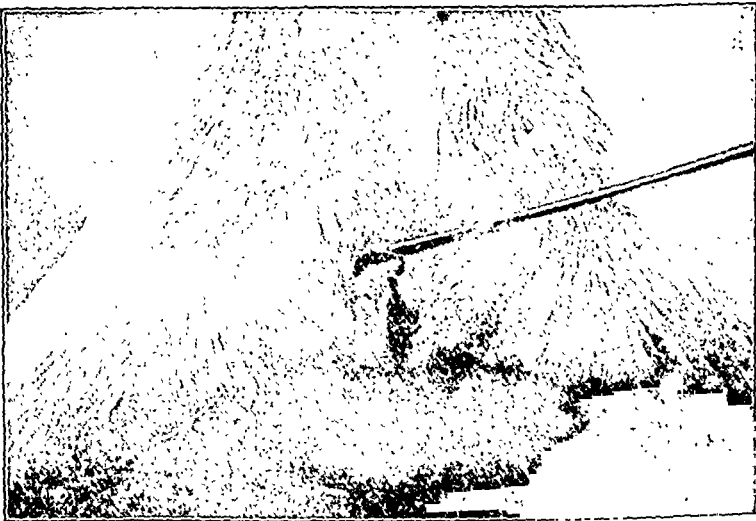


Fig. 21.—Normal male (brother).

the close of this, already having developed male characteristics. Even in the case of animals where the signs of sex are as fixed as this, they can be operated upon and changed.

I have not yet succeeded in producing the phenomena in animals as old as a year, but incline to believe in the possibility of doing so in view of the experiments of Pézard on fowls (J. de physiol. et de path. gén., 1922).

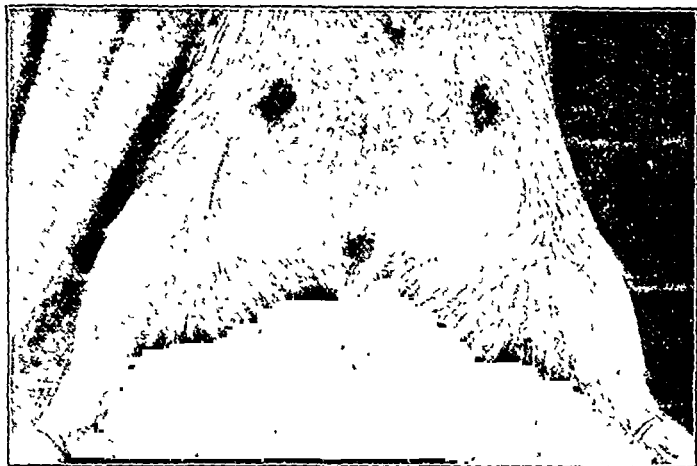


Fig 22 —Normal female (sister).



Fig 23

Figs. 20, 21 and 22 show a puberty series of this type in the same litter. The experimental hermaphrodite, the normal male (brother), and the normal female (sister). As can be seen, the

Some microscopic discoveries will also be given. Fig. 23 shows the beginning of the processes after 3 weeks' time, the ovaries were preserved with a copious supply of blood vessels

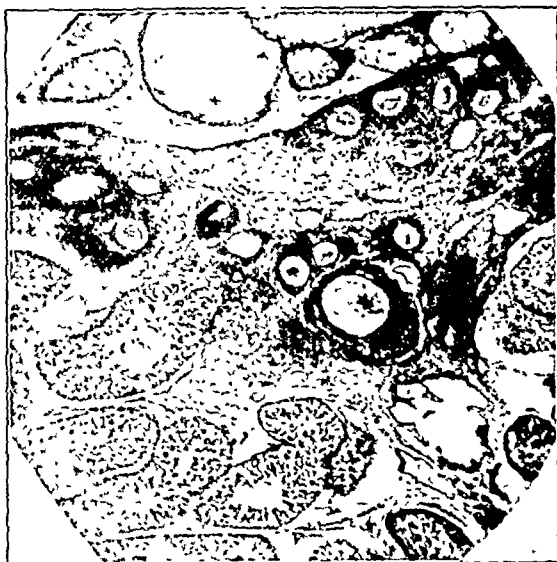


Fig. 24

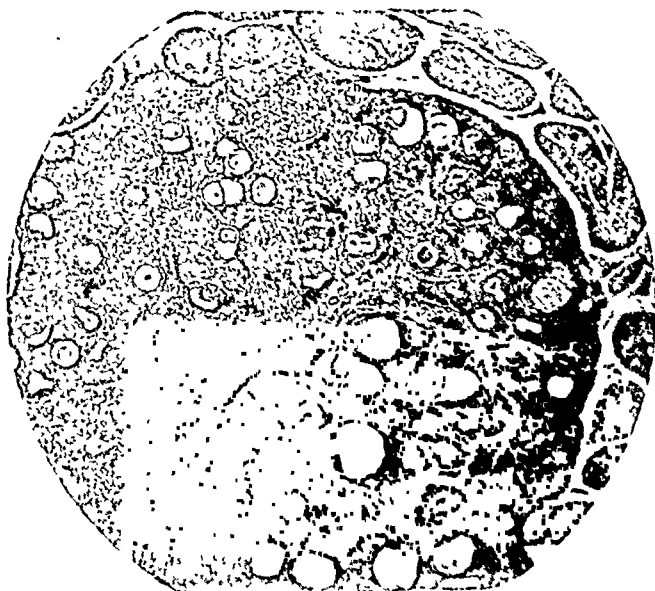


Fig. 25

passing in from the testis tissue. Fig. 24 shows a rather badly preserved ovary in normal testis tissue with spermatogenesis, for the most part consisting only of atretic follicles with theca

lutein tissue, but still with complete ovariostestis (combined hormone) influence in hermaphrodite respects. Fig. 25 stands out in striking contradiction to this, showing an even unusually well-preserved ovary also in normal testis tissue, but in endocrine respects the ovary portion (part played by the ovary) had not influenced the animal at all here, in spite of its excellent condition.

This very strange phenomenon, practically unexplainable at the moment, and which I have observed in 4 cases, gives much food for thought with regard to the endocrinology of the sexual glands and calls upon us to exercise the greatest prudence, and not least with regard to the question which we shall in conclusion briefly touch upon here.

THE PLACE OF PRODUCTION OF THE SEXUAL HORMONES

With regard to the general endocrinology of the sexual glands a fair degree of clearness has been reached through the important experiments of the last decades. No one would think of denying that in the endocrine makeup of the body the sexual glands act in intimate coordination with numbers of other endocrine glands; we now know too well their reciprocal correlations and their reciprocal indispensableness for that.

On the other hand, no one doubts, either, that the gonads as endocrine glands manifest hegemony and have strange power over the organism through their hormones alone. All of the fundamental research on transplantations, injections, castrations, transformations, experimental hermaphroditism, etc., have fully shown this. And for the physiologists, especially endocrinologists, these must be the main and most interesting points, which, of course, they always are for the majority and for those who possess the deepest biological knowledge.

The question as to which tissues produce the hormones must always remain a subordinate question, even though it may be of the greatest interest morphologically.

But with regard to this question opinions do not agree so well as with the endocrine. As far as my own viewpoint goes, spatial limitations require me merely to refer to my earlier publications (especially in *J. de physiol. et de path. gén.*).

It is in Germany particularly that the question concerning what is understood by the idea which the French call "glande

interstitielle," which Steinach names "Pubertaetsdruese," and which I have suggested calling by a neutral word, "sexual hormone tissue," has given rise to much controversy and innumerable articles, certainly not all equally finished in form nor of great scientific value.

It seems at present as if this controversy, wrongly as a matter of course, is overshadowing the much more interesting physiological questions, and it cannot be denied that, to a neutral and unprejudiced observer, it gives the impression of being rather biased. This controversy seems to be specially taken up with what the Germans call "Steinach's Pubertaetsdruesenlehre." As I have often emphasized, "Pubertaetsdruese" is, in fact, an unfortunate term, but it is after all only a word, and perhaps during the rapid development of sexual endocrinology, also theories and conclusions which have been put forth, will later have to be revised.

It is to be noted that all of these substantially new and theoretical authors who come forward, for the most part as Steinach's opponents, seem to forget that the theory of the special hormone tissue in the gonads comes originally from French scientists (Prenant, Livon, Bouin and Ancel and others). Furthermore, by no means all of the arguments offered are new or well-founded, and many of these articles, whose number will soon be legion, contain astonishing misunderstandings and erroneous reports.

It is not my intention here to enter further into the subject of this controversy. I will only add that, for example, with reference to Leydig cells ("die Leydigfrage"), nearly all the arguments are the old ones well known as early as Bouin and Ancel's period (1903), and still justly valued by later scientists (Tandler, Grosz, Steinach, Athias, Lipschütz, Sand, etc.).

In reality no new points of vital importance have arisen which, with regard to mammals, can change the opinion that the Leydig cells have, besides their nutritive function, great, perhaps the very greatest, importance for the hormone production of the testis. Of this most of the moderate scientists are certainly now convinced.

This theory, founded originally on Bouin and Ancel's ingenious experiments, has, through continuous transplantation experiments, vasoligations, experimental cryptorchism, etc.,

found further support, more plentiful and convincing at any rate than the support, which even at best is small, to be found for the theory of the generative tissue as the only hormone producer in mammals. There is great danger in attempting to generalize regarding the different classes of animals in this respect, as many do, and draw conclusions from one class as applying to the other. They can at best only throw light mutually on each other's conditions.

As on so many other points, absolute certainty has hardly been reached here, and will perhaps not be arrived at, but a good deal of progress has been made.

With these few concluding words it has been my wish only to invite moderation and clearness on all sides, without losing oneself in the less important questions of detail. Sexual biology still contains many problems which are waiting to be solved, and both for those who have hitherto worked in these fields and for those who purpose to take up the work, there is every reason not to lose sight of the headlines, but in spite of periodical controversies, which will always come up, continue to work steadily and soberly on the lines which, up to now, have been found to lead to fruitful and important results.

BIOLOGICAL AND ANATOMICAL STUDIES OF THE NUPTIAL EXCRESCENCE AND BIDDER'S OR- GAN OF THE TOAD (BUFO BUFO JAPONICUS—SCHLEGEL)

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Bidder's organ has been described by a number of writers, among whom are Rüssel von Rosenhof (1758), Rathke (1825), Jacobson (1825), Bidder (1846), v. Wittich (1853), Leydig (1853), Spengel (1876), A. M. Marshall, Bourne, and M. Nussbaum (1880). In 1886 Emil Knappe published a detailed work on Bidder's organ, but could not give any satisfactory explanation of it. He was followed by others, among whom may be mentioned Hoffman (1886), Ognew (1907, who includes an account of the report of Cerruti), Aimé (1908), King (1908, 1910), and Harms (1913). Bidder's organ has been morphologically and histologically most minutely investigated, but no general agreement has been reached concerning its significance.

The various opinions of writers in regard to Bidder's organ may be classified into four groups: 1. Bidder's organ is a rudimentary ovary (Jacobson, von Wittich, Bourne, Marshall, etc.); 2. Bidder's organ is a part of the testis (Bidder), or a preparatory sexual organ (Spengel); 3. The significance of Bidder's organ has not been determined (Knappe, King, etc.);

4. Bidder's organ prepares a kind of hormone and shows special characteristics (Harms).

A minute description of this organ is given by Bidder, who describes the connection between the germ gland and Bidder's organ, especially in regard to the blood supply. All attempt to give the biological significance of Bidder's organ, which is found only in anamniotes, has failed. It has been considered an enigma from antiquity to the present time.

Certainly, the nuptial excrescence (Bidder's organ) shows anatomical and histological differences according to the time of development. This is especially evident in the case of the common frog (Bufo communis).

experiments,

amination, since it undergoes a cyclic transformation closely related to the period of sexual activity.

During the nuptial period the excrescence is macroscopical, velvet-like, coal black and glossy. It is slightly higher than the surrounding skin level and presents a surface which is provided with several small elevations. After the mating season it gradually disappears, i. e., it loses its blackish color, and the hand is apparently not to be distinguished from that of the female, but upon closer examination several minute elevations are to be seen, even in the resting stage. The cornified layer of the epithelium covering the protuberance consists, according to the reports of Harms, of a single layer of cells. Upon the excrescence are to be found a number of large barbed hooks.

The nuptial excrescence of the thumb presents a transitional form between the real gland of the thumb callosity and the mucous type of gland, the latter of which is generally to be found in the skin.

Bidder's organ originates from the germ cells, differentiates earlier than the germ gland, shows the histological structure of a rudimentary ovary and is to be found in both sexes at an early stage. That of the female disappears after a certain time, while that of the male persists.

Bidder's organ of *Bufo bufo japonicus* (Schlegel) undergoes a definite transformation cycle. In the spring it is very poorly developed, in June its development is complete, and in the second half of the winter it undergoes involution.

Bidder's organ is placed symmetrically on both sides of the vertebral column, ventral to the kidney and between the corpus adiposus and the testes. It is oval or heart-shaped, and flattened, and its surface is granulated. Sometimes it is cylindric like the testis and closely connected with the latter, as if it were a part of it. But even in this case we can easily distinguish between the two by the difference in color. Bidder's organ being a reddish-yellow and the testes a blackish-brown.

The animals used for my experiments were nearly all adult and weighed between 130 and 170 grams. In only a few cases was use made of young individuals (8 to 20 grams), it being found useless to employ the young animals for these experiments.

The experiments which I have undertaken consist in the extirpation of Bidder's organ and of the germ gland, followed by observation of the secondary sexual characteristics, especially the excrecence of the thumb. There were over 300 experiments but I report here only a summary of the results obtained. Care was taken that the experimental animals live under the same conditions after the operation as before, and I succeeded in maintaining them in a good state of nutrition.

I have been able to prove that the nuptial excrecence of *Bufo bufo japonicus* (Schlegel) is a secondary male sexual characteristic standing in close relation to a germ gland. By the extirpation of both the testes and Bidder's organs the development of the excrecence could be completely stopped or even reduced to degeneration, while a regeneration could be observed by transplantation or subcutaneous injection of the germ gland.

The effects produced differed gradually according to the germ gland employed and diminished in the following order: Testis, ovary and Bidder's organ.

All experiments with injections or feeding of various other organs gave negative results.

Most probably Bidder's organ is an internally secreting organ which is able to influence the secondary sexual characteristics of the toad (*Bufo bufo japonicus*—Schlegel), however, its influence is somewhat less than that of the testes.

PILOCARPINE AND ATROPINE TESTS—HAND SET PILOCARPINE AND ATROPINE IN FUNCTIONAL EXPLORATION OF THE VISCERAL- NERVOUS SYSTEM.

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We have already proved (1), in contradiction to Goetsch's statement (2), that the reaction provoked by a subcutaneous injection of 0.5 mg. of adrenaline is not specifically due to a state of hyperthyroidism, but that the hyperfunction of the thyroid gland can exaggerate the action of adrenaline. We consider accelerated heart beat after its administration a sign of sympathicotonia.

Here we will express briefly our opinion on the use and significance of pilocarpine and atropine in functional exploration of the visceral nervous system.

Patients were systematically observed in the following way. A close and complete clinical examination was carried out, with especial regard to endocrine glands and visceral nerves. Temperature and weight variations were recorded. During a week, every day at the same hour, patients were taken from the ward to a small, quiet room and comfortably accommodated in supine position, being allowed to read indifferent literature. Every 10 minutes for an hour pulse rate and blood pressure were recorded. On the eighth day pilocarpine or atropine was injected. When using the first drug, blood pressure, quantity of saliva secreted, pulse rate, place and quantity of sweating and subjective sensations were noted. With the second, pulse rate, state of pupils and subjective sensations were recorded.

PILOCARPINE

Eppinger and Hess (8) consider this drug as having a special affinity for parasympathetic nerves (cranial and sacral portion of autonomic system). Subcutaneous injection of 0.01 gm. would provoke, in cases of vagotonia, sweating, increased

salivary secretion and subjective symptoms. To explain the action on sweat glands they consider them as innervated by parasympathetic nerves, though anatomical data contradict this statement.

Up to this time nobody has given a definite proof of the existence of this special affinity. Frank (3) postulates the existence of parasympathetic nerve fibres in the paravertebral sympathetic ganglia but gives no data to sustain his assertion. Pottenger (4) and Guillaume (5) discuss contradictory opinions without adopting any one of them definitely. Müller (6) accepts Dieden's experimental results on double innervation of sweat glands and admits an elective affinity of pilocarpine for parasympathetic nerve fibres. It is curious that on such an important point, authors should either accept Eppinger and Hess' ideas without control, or pass them in silence, with the exception of Lurá (7), whose work will be mentioned later.

Taking all necessary precautions to avoid errors as we have done on other occasions (9), we have determined the *useful test dose*. Most authors use 0.01 gm. according to Eppinger and Hess' instructions. We have obtained the following results with 2.5 and 10 milligrams:

No. of Cases	Dose	Sweating	Per Cent	Salivation	Per Cent
86	0.002	10	11.6	52	60.4
80	0.005	27	33.7	61	77.5
172	0.01	110	63.9	153	89.2

With 2 mg. a great number of patients have increased salivary secretion but only a few sweat. With all doses salivary secretions predominate. Percentage of sweating is in direct relation to the dose employed; this relation does not exist with regard to salivation.

We can conclude, therefore, that salivary glands have a special susceptibility to pilocarpine and that sweat glands are influenced in a smaller degree. This is due to difference in innervation, parasympathetic (corda tympani) for salivary glands, sympathetic for sweat glands.

In accordance with these observations we believe that pilocarpine has not an *elective* action on parasympathetic nerves, as Eppinger and Hess and those authors that accept their views affirm, but simply a *predominant* action. For this reason we prefer lower doses and consider 2 milligrams injected subcu-

taneously as an adequate dose to explore parasympathetic irritability, considering it increased when salivary secretion attains 50 cc. and more.

Sweat glands have only one class of nerves, being an exception to other glands that receive nerves from both sections of the autonomic system. Their susceptibility to sympathomimetic and vagotropic drugs is a physiological adaptation; sweating is for this reason observed in cases that correspond to an increased tone of either system.

Pilocarpine acts also on the circulation. Lurá first observed that this drug has an action similar to that of adrenaline, but in a smaller degree. His assertions are supported by a small number of observations. According to Müller bradycardia is observed.

In 97 cases we have obtained the following results:

Tachycardia	29	29.8%
Bradycardia	4	4.1%
No difference	64	65.9%
—		
97		

We speak of tachycardia when there is an increase of 10 heart beats per minute. It commences soon after injection and lasts half an hour. Variations in blood pressure are not constant and palpitations are rarely observed. Frequency of tachycardia diminishes with dose; with 2 mg. it is never observed. There is no relation in degree between circulatory variations and salivation or sweating.

This circulatory action can only be explained by irritation of sympathetic nerves. It has no clinical significance. It is not consistent with Eppinger and Hess' affirmation on elective action of pilocarpine on parasympathetic nerve fibres.

SUMMARY

1. Pilocarpine acts on both sections of the autonomic nerve system; it provokes increased salivary secretion through parasympathetic and sweating through sympathetic nerve fibres.
2. Sweating provoked by the injection of 0.01 gm. pilocarpine is no proof of parasympathetic innervation of the sweat glands.

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THE CALCIUM CONTENT OF THE BLOOD OF THYROIDECTOMIZED ANIMALS

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One of the most important functions of the thyroid is the regulation of the calcium metabolism of the organism. The absence of the thyroid secretion produces marked disturbances in the osseous system so that the animal is unable to assimilate calcium save to a very slight extent. Numerous investigators have worked on the problem, but without reaching concordant results. We have accordingly restudied the problem, investigating the calcium content of the blood of three sheep thyroidectomized at the age of six weeks. Controls of the same age or thereabouts were raised with the test animals. The blood for analysis was taken one year after operation. The calcium was determined according to Neumann's method. The results are given in the accompanying table. It is seen that the calcium content of the blood in the thyroidectomized animals is less than that of the normal controls. Thus 1 Kg. of fresh blood of the normal animal contained about 0.07 grams calcium and 1 Kg. dried blood about 0.36 grams; while in the blood of the thyroidectomized animals there was about 0.053 grams per Kg. in the fresh blood and 0.270 grams in the dry blood. This calcium diminution in the blood of the thyroidectomized animals may explain in part the tendency to hemorrhage in thyroidal insufficiency. Likewise one can possibly attribute to calcium deficiency such disorders as urticaria, pruritis and eczema which have developed on a hypothyroid terrain. These disorders disappear on thyroid opotherapy, which apparently regulates the calcium or the organism in determining its retention, a result similarly attained by treatment with calcium salts.

TABLE
(Experiments on normal sheep)

Date	Wt. of Animal Kilos	Wt. of Fresh Blood Grams	Wt. of Dry Blood Grams	Water Content of Fresh Blood in 1000 Grams	Total Calcium Grams	Calcium in 1000 Grams Fresh Blood, in Grams	Calcium in 1000 Grams Dry Blood in Grams
June 15....	63	20.894	3.971	810	0.0015	0.071	0.380
June 20....	55	18.987	3.719	804	0.0013	0.068	0.350
June 26....	57	22.405	4.503	799	0.0016	0.071	0.360
Average						0.070	0.360
(Experiments on thyroidectomized sheep)							
June 15....	51.300	21.912	4.207	808	0.0012	0.054	0.280
June 20....	36.200	26.425	4.974	811	0.0013	0.049	0.260
June 26....	44.100	17.995	3.383	812	0.0010	0.056	0.290
Average						0.053	0.270

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CORRELATION BETWEEN CREATININE AND TOTAL NITROGEN ELIMINATION IN TWO CASES OF DYSTROPHIA ADIPOSO-GENITALIS

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Introduction: The creatinine elimination of man has been the subject of much study and many experiments by physiologists and chemists and the literature on this interesting urinary constituent is quite extensive. Practically all investigators since the publication of Folin's colorimetric method for the determination of creatinine are agreed that the amount eliminated by any individual is practically constant from day to day. Folin (1) says, "The absolute quantity of kreatinin eliminated in the urine on a meat-free diet is a constant quantity different for different individuals, but wholly independent of quantitative changes in the total amount of nitrogen eliminated." This conclusion has been fully confirmed by Von Hoogenhuyze and Verploegh (2), Klercher (3), Closson (4), Shaffer (5), and others.

With this fact so firmly established we were very much surprised to find so wide a variation in the daily creatinine output of two patients suffering from dystrophia adiposo-genitalis, who also manifested the further peculiarity of a close correlation between the creatinine and total nitrogen elimination. As a check on our work we analyzed the urine of a normal individual for a few days and found the creatinine output constant.

The variation in the daily creatinine output described in this paper was noticed during a study of the effects of treating the above patients by intramuscular injections of tethelin. The result of the tethelin treatment will be published later.

Method of Collection and Analysis: The twenty-four hour specimens were collected by having the patients void their urine directly into clean bottles containing chloroform for a preservative. Care was taken that no urine should be lost. On several occasions when we had reason to believe that some urine was lost we rejected the analyses. The analyses were always started

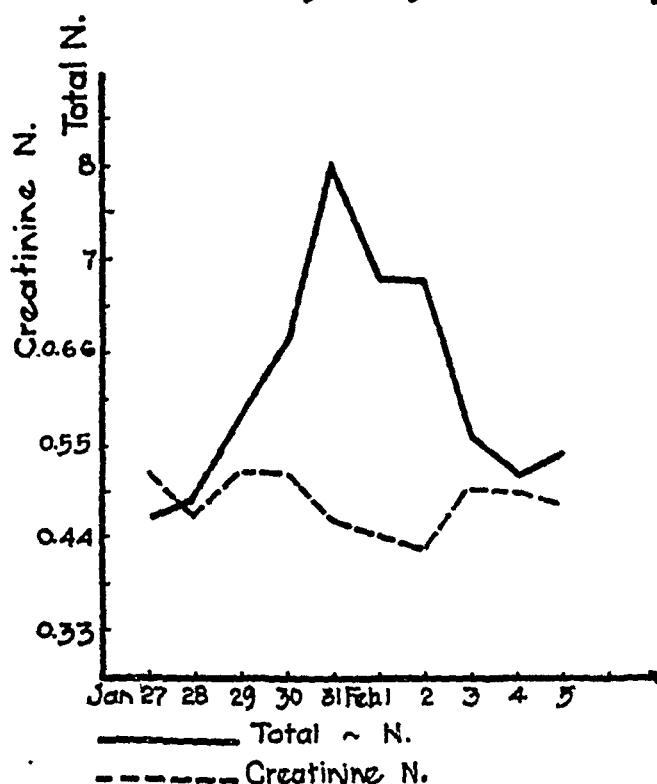
within two hours after the final micturition of the twenty-four hour period.

The total nitrogen was determined by the Kjeldahl method (6) and the creatinine and creatine by the colorimetric method of Folin (7).

Both patients were on a diet consisting of eggs, bread, oatmeal, fruit and milk. We had some difficulty in keeping patient

Figure-1~

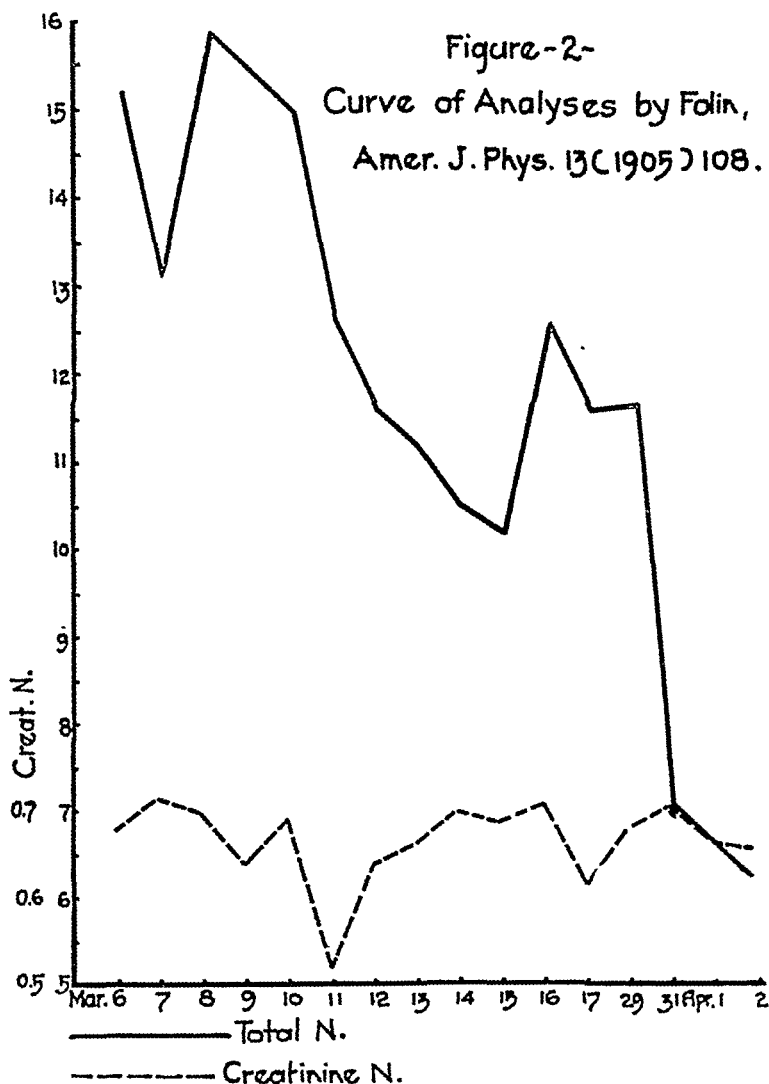
Curve of Analyses by Folin. Am. J. Phys. 13 (1905) 70



J. C. on the diet and he frequently obtained food from the other patients in the ward. This fact accounts for the wide variation in his total nitrogen output, but cannot be said to have affected the creatinine output because patient T. J., who adhered to the prescribed diet, shows the same type of creatinine output as

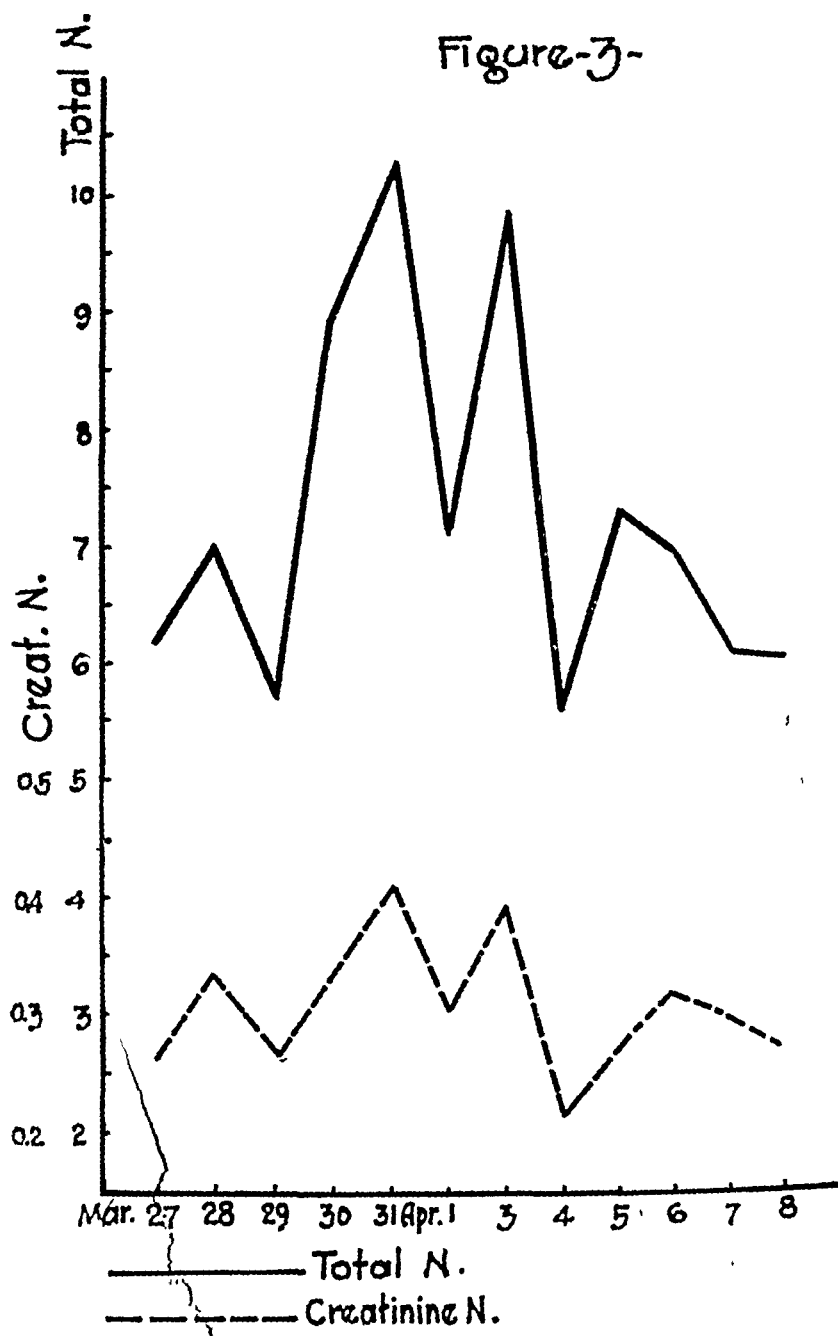
J. C. Both patients took a moderate amount of exercise every day.

Discussion: A study of the following tables and curves will show that the creatinine output was not constant and that it

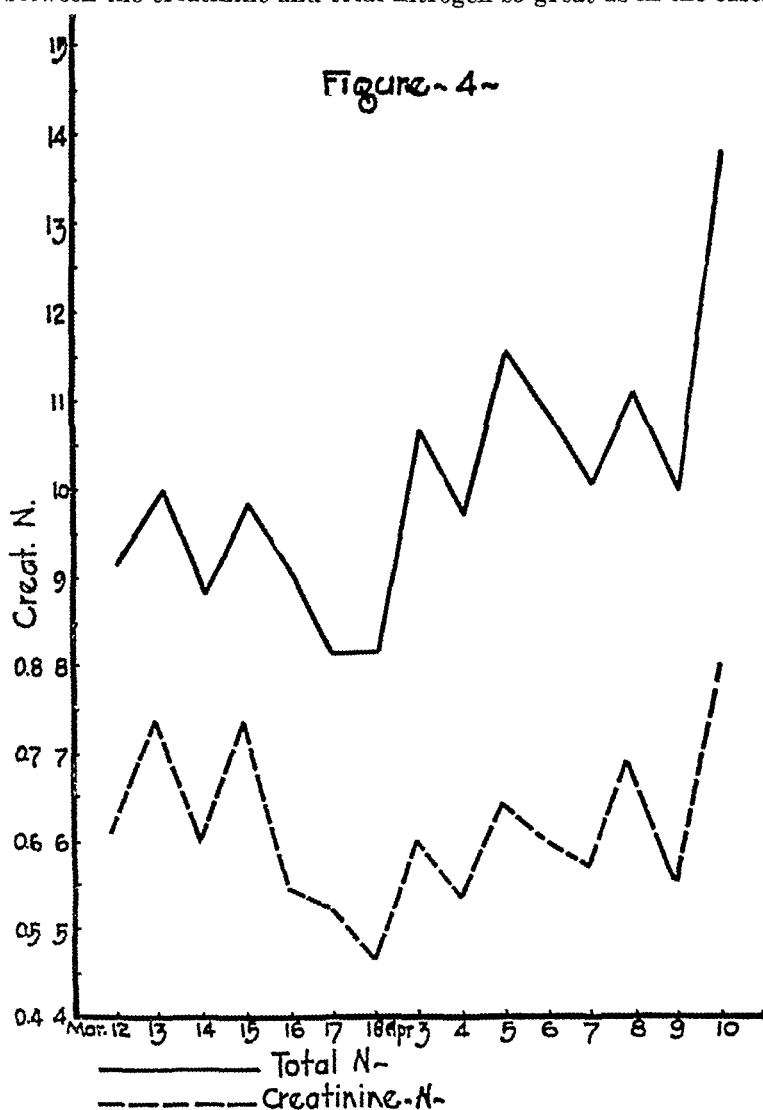


varied with the total nitrogen. This variation is made more striking by comparison with a standard of normal metabolism. For this purpose we have made curves from two tables of Folin

(8), which we believe furnish accurate knowledge of the amount of creatinine in normal urine. Curves 1 and 2 were made from the figures published by Folin and 3 and 4 from our results.



A review of the results of many observers leads us to the conclusion that in disease the creatinine output is not constant, as it is in health, but in no case have we found the correlation between the creatinine and total nitrogen so great as in the cases



here reported. Shaffer (9) has shown that a low excretion of creatinine is found in many pathological conditions and that the excretion of an abnormally small amount is not peculiar to

any one disease. In these two patients the creatinine coefficient is low, but this is to be expected because both were excessively fat.

Practically all investigators are agreed that the amount of creatinine excreted is an index of muscular efficiency. We have no proof, however, that creatinine arises wholly in the muscles, but that it does arise there, in part at least, may be considered proven.

Experiments by Gottlieb and Stangassinger (10) appear to indicate that the formation of creatin and creatinine takes place in the glandular organs as well as in the muscles.

Our own results seem to indicate that the pituitary body has some controlling influence on creatinine excretion, either by controlling its rate of formation or its elimination.

It is possible that it is characteristic of hypofunction of the pituitary gland that the creatinine output should vary concomitantly with the total nitrogen. With our two cases, however, it is not possible to make a generalization, but only a suggestion of what may prove to be a pathognomonic sign.

TABLE 1
(For Curve see Figure 3)

Date	Total N.	Creatinine N.	In % Total N.
Mar. 27.....	6.20	0.36	4.2
Mar. 28.....	6.98	0.33	4.7
Mar. 29.....	5.74	0.26	4.5
Mar. 30.....	8.91	0.33	3.7
Mar. 31.....	10.38	0.41	3.9
Apr. 1.....	7.13	0.30	4.2
Apr. 3.....	9.94	0.40	4.0
Apr. 4.....	5.56	0.21	3.8
Apr. 5.....	7.37	0.27	3.5
Apr. 6.....	7.00	0.32	4.6
Apr. 7.....	6.20	0.30	4.8
Apr. 8.....	6.09	0.27	4.4

TABLE 2
(For Curve see Figure 4)

Date	Total N.	Creatinine N.	In % Total N.
Mar. 12.....	9.29	0.63	6.7
Mar. 13.....	10.02	0.74	7.3
Mar. 14.....	8.88	0.60	6.7
Mar. 15.....	9.88	0.74	7.5
Mar. 16.....	9.07	0.55	6.1
Mar. 17.....	8.20	0.53	6.3
Mar. 18.....	8.23	0.46	5.6
Apr. 3.....	10.77	0.60	5.5
Apr. 4.....	9.70	0.54	5.5
Apr. 5.....	11.59	0.64	5.5
Apr. 6.....	10.93	0.60	5.5
Apr. 7.....	10.07	0.56	5.6
Apr. 8.....	10.22	0.58	5.7

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2. Von Hoogenhuyze & Verploegh: Ztschr. f. physiol. Chem. (Berl. & Leipz.), 1905, 46, 415.
3. Klercher: Biochem. Ztschr. (Berl.), 1907, 3, 45.
4. Closson: Am. J. Physiol. (Balt.), 1906, 16, 252.
5. Shaffer: Am. J. Physiol. (Balt.), 1908, 22, 445.
6. Hawk: Practical Physiological Chemistry, 512. 1907, P. Blakiston's Son & Co.
7. Folin: Ztschr. f. physiol. Chem. (Berl. & Leipz.), 1904, 41, 222.
8. Folin: Am. J. Physiol. (Balt.), 1905, 13, 45-66.
9. Shaffer: Am. J. Physiol. (Balt.), 1908-09, 23, 1.
10. Gottlieb & Stangassinger: Ztschr. f. physiol. Chem., 52-55.

Book Reviews

/ **PHYSIOLOGIE UND PATHOLOGIE DER HYPOPHYSE.** Prof. Dr. Artur Biedl, Prag, 1922. Verlag von J. F. Bergmann, 81 p.

With his well known clarity of diction Professor Biedl has discussed the hypophysis in its normal and pathological relationships, from both the anatomical and pathological points of view. A considerable number of excellent original illustrations are included. To anyone desiring a brief, up-to-date discussion of the subject, this little book can be highly recommended.

—R. G. H.

/ **LE DEBOLEZZE DI COSTITUZIONE—INTRODUZIONE ALLA PATOLOGIA COSTITUZIONALE. PARTE I. CONCETTI GENERALI.** Nicola Pende, Ed. Libreria di Scienze e Lettere, Roma, 1922.

Prof. Pende discusses in this monograph the various forms of constitution and the somewhat confusing nomenclature as found in the German as well as the French literature. He comes to the conclusion that all of the types can be brought to the three chief classifications of Viola, *i. e.*, normal, megalosplanchnic and microsplanchnic. The volume, some 136 pages altogether, is very interesting, as the classification is based on anthropometric measurements.—G. V.

/ **MORBO DI HIRSCHSPRUNG E NANISMO IPOFISARIO.** Prof. Dott. Nino Samaja, Primario e Libero Docente. Paper, pp. 52. Pesaro: Prem. Stab. d'Arti Grafiche Cav. G. Foederici, 1920.

Reviewed in J. Am. M. Ass., 1921, 77, 1042.

Abstract Department

(ADRENALS) Las capsulas suprarrenales en la clinica terapeutica. Alou Bernat (P.), Union méd. (Zaragoza), 1921, No. 197, 553-556.

A brief résumé of the physiology and pathology of the suprarenals with report of a case of Addison's disease.—E. B.

The involution of the zona reticularis in the ADRENAL gland of the infant (Sulla involuzione della zona reticolata nella ghiandola surrenale del bambino). Ausenda (C.), Osp. maggiore (Milano), 1920, 8, 162-170 (August).

Following the observations of recent investigators the author accepts for the adrenal cortex a functionally homologous structure, in spite of the anatomical division of the cortex in three zones. This explains the vicarious function of the several zones in pathological conditions of adults as well as the morphological modifications seen in the zona reticularis during the first year of life. During this period the zona reticularis of the infant tends to disappear completely, owing to a process of normal involution. In its stead the medullary substance grows in proportion to the disappearing of the zona reticularis. Its function is temporarily undertaken by the zona fasciculata in its period of speedy development. What is left of the zona reticularis at the end of this process is a connective-vascular zona, forming a boundary between the cortex and the medulla. It can be seen even in a 5 year old child. As soon as this disappears the cortex and medulla come in contact. With increasing age a new zona reticularis is formed by the zona fasciculata, and in adults reaches full growth. Syphilis seems to delay its involution. Nothing is known of the function of this normal involution or the eventual relations between this period of the adrenal gland and the other endocrine organs.—G. V.

Infantile tolerance of ADRENAL extract (Tolerancia infantil a la suprarrenina). Blanco Soler (C.), Arch. españ. de pediat. (Madrid), 1922, 6, 146-150 (March).

A girl, aged 4 years, was given 20 to 30 drops daily of suprarenal extract for 26 months without exhibiting the least symptom of intolerance. The author interprets this circumstance as another proof of the inefficacy of ingested suprarenal extract.—G. M.

(ADRENALS) Endocrine studies (Cronica de endocrinologia). Bonilla, Méd. ibera (Madrid), 1921, No. 176, 226-288.

A criticism of the ideas of Gley concerning the physiology of the suprarenal capsules.—G. M.

(ADRENAL) Postinfluenzal Addison's disease (*Un caso de Addison post-gripal*). Bonilla, Méd. ibera (Madrid), 1921, No. 214, 456-458.

A typical case of Addison's disease appeared immediately following a severe attack of gripe in a previously healthy girl of 18 years. The patient was temporarily relieved by anti-influenzal vaccine, but finally died. Notwithstanding the fact that suprarenal lesions have been encountered at autopsy following gripe (Sergent, Marañón), there appears in the literature but one case of post-influenzal Addison's disease, reported by Brunecke [Therap. Monatsh. (Berl.), 1919, 33, 354].—G. M.

A primary tumor in the liver of probable ADRENAL origin (*Sopra un tumore primitivo del fegatodi probabile origine cortico-surrenale*). Cirio (L.), Pathologica (Genova), 1922, 14, 197-207 (April).

A necropsy report of a case of abdominal tumor closely connected with the free margin of the liver. The normal condition of both surrenal cortexes excluded the hypothesis of metastasis. From the external characteristics as well as from histological findings the tumor was diagnosed as a blastoma of adrenal cortex origin and was classified as carcinomatous.—G. V.

Sifilis y capsules suprarrenales. Covisa (J. S.) & Bejarano (J.), Soc. españ. de dermat. y sifil. (Madrid), 1921.

In subjects affected with syphilis and in whom asthenia and pigmentation appear, hypotension is always present, which is regarded as indicating suprarenal hypofunction. In such cases, besides energetic antisiphilitic treatment, adrenalin is said to be indicated.—E. B.

Ulcera de estomago y hipofunction suprarrenal. Echevarria Martinez, Aragon méd. (Zaragoza), 1922, 52, 1-6.

In a case of gastric ulcer the author found symptoms of suprarenal insufficiency (hypotension, asthenia and melanoderma), mononucleosis absolute and relative, and vagotonia. He describes the relations which exist between hypoadrenia and gastric ulcer. In Addison's disease there are always symptoms that affect the digestion, and in autopsies in such cases the author frequently encountered erosions and even true gastric ulcers. Finzi has demonstrated these lesions in dogs after having extirpated the suprarenals. These conditions are explained by the increase of the tonus of the vagus, which determines the increase of gastric secretion, contraction of the muscularis mucosa and spasm of the pylorus.—E. B.

ADRENAL factor in the vaso-motor reactions following splanchnic stimulation [*La fonction des surrénales. Nouvelles recherches sur*

l'action vaso-motrice du nerf grand splanchnique chez quelques Mammifères (Ongulés et Rongeurs)]. Gley (E.) & Quinquaud (A.), *J. de Physiol. et de path. gen.*, 1922, 20, 193-199.

The two-step rise of pressure, seen characteristically in the dog and cat on stimulating the splanchnic nerve, and rarely seen in the rabbit, was studied further in the rabbit, and the study was extended to the viscacha, the goat, the horse, the mule and the cow. The rise was found to be more or less inconstant according to the species of animal. The authors conclude that the inconstancy is scarcely favorable to the idea that the second step in the rise of blood pressure is always dependent on adrenal secretion, or if adrenal secretion is evoked by splanchnic stimulation that it produces a physiological effect in every case.—W. B. C.

The influence of the ADRENAL cortex on the growth and the reproduction of lower organisms. v. Herwerden (M. A.), *Proc. Konink. Akad. v. Wet. (Amsterdam)*, 1922, 33, 1339-1342.

The addition of adrenal cortex to water in which *Daphnia pulex* is being bred appears to stimulate growth and make the cultures more resistant to such conditions as over-population, inadequate supply of oxygen, and the growth of moulds and of multicellular algae.—*Physiol. Abst.*, 7, 340.

(ADRENAL) A case of Addison's disease with atypical development (Un caso de enfermedad de Addison con evolution atypica). Juarros (C.), *Prog. clin. (Madrid)*, 1922, No. 122, 252-255.

A case is reported of a patient, 22 years of age, with no history of sickness except attacks of malarial fever, after which he had swelling of the legs and abdomen, loss of strength and general malaise. Some months afterwards the patient presented a typical syndrome of Addison's disease, his digestive apparatus being much affected (vomiting and diarrhoea). He was put on a diet of milk and boiled eggs and given, at the same time, adrenalin. He improved notably during the next few days. Upon return to normal diet, however, the symptoms became so severe that he was obliged to return to the milk and egg diet.—E. B.

(ADRENALS) Biochemical studies of the origin of typhus immunity (Biochemische Untersuchungen über die Entstehung der Typhus-immunität). Kanai (T. J.), *Biochem. Ztschr. (Berl.)*, 1922, 132, 26-52.

After the intravenous injection of typhus bacilli and typhus toxin in rabbits, the rest—N of the blood and the total N of the urine fluctuate proportionally with the leucocyte count. The immunized typhus blood contains a specific substance which reacts like adrenin upon the eye of the frog, the pupil of the rabbit, the blood

vessels of the frog and the rabbit uterus. Typhus bacilli and toxin have quite the opposite effect. When they are injected intravenously there is produced a significant inhibition of adrenal function, while on the other hand pneumococci and colon bacilli have a significant stimulating effect as measured by the reaction on the surviving rabbit eye. Immunity arises after the intravenous injection of typhus bacilli, when the leucocyte count and rest—N of the blood and the adrenin or adrenin-like substance are found to be increased. The condition of hyperglycemia caused by the injection of a pathogenic organism is probably due to increased adrenal function. In vitro experiments failed to demonstrate the ability of typhus bacilli to form an adrenin-like substance in protein medium directly from l-tyrosin, p- or o- "hydroxyphenylbrenztraubensäure," or p-hydroxyphenyl lactic acid.—F. S. H.

(ADRENAL) The importance of cholesterin in infectious diseases (*Die Bedeutung des Cholesterins bei Infektionen*). Leupold (E.) & Bogendorfer (L.), *Deutsche Arch. f. klin. Med.* (Leipz.), 1922, 140, 28-38.

During infectious diseases the adrenals generally contain only small quantities of cholesterin, caused, the authors believe, by the small quantities of cholesterin found in the blood during these diseases. They believe that the toxins come into the blood from a non-toxic compound. Small doses (50-100 mg. daily) of cholesterin were given to rats, mice and guinea pigs for 3 to 4 weeks. Their resistance was much greater than that of the control animals.—J. K.

ADRENAL cortex ablation (*Contributo allo studio delle capsulopatie sperimentali*). Lucibelli (G.), *Folia med.* (Napoli), 1920, 6, 337-343; abstr., *Pathologica* (Geneva), 1922, 14, 93 (February).

When one whole capsule and one-half of the other is removed in rabbits the animals die with slow asphyxia, which resembles very much the asphyxia of hypoadrenalism. The half capsule left does not compensate for the loss. The myocardium of these animals is in poor condition as well as the cardiovascular pressure and the constitution of the blood.—G. V.

(ADRENAL) Mast cell leukocytosis in a case of Addison's disease (*Mastleucocitosi del sangue in un caso di morbo d' Addison*). Maiolo (B.), *Rassegna internaz. di clin. e terap.* (Napoli), 1922, 3, 137-146 (April).

After a discussion on the changes in the blood due to the action of the endocrine glands the author reports a case of Addison's disease in which the Mastzellen percentage reached 9%. He believes that this finding, if not of diagnostic, is at least of clinical importance.—G. V.

The ADRENALS in experimental anemia (*Comportamento della surrenale nelle anemie sperimentali*). Marino (S.), Arch. farmacol, 1920; abst., Pathologica (Genova), 1922, 14, 93-94 (February).

The fat substances of the adrenal cortex behave differently in hemolytic poisoning than after blood letting. In the first case the esters of glycerin and of cholesterol predominate in the lipoids; the opposite is true after blood letting. The pigment is in great abundance in the two series of animals, but in quality it does not differ from the pigment found in normal conditions and there is nothing to lead us to conclude that it is of hematic origin.—G. V.

Quantitative relations of the ADRENALS to the remainder of the body (*Die quantitativen Beziehungen der Nebennieren zum übrigen Körper*). Schief (F.), Ztschr. f. Konstit. (Berl.), 1922, 8, 507-544.

This report is based on autopsy material gathered at Jena from 423 males, 18 to 51 years old, and recently engaged in active army service, and on 804 civilian autopsies performed before the war (during normal conditions of food supply, etc.). The civilian series includes both sexes, all ages up to 90 years, practically every vocation from both rural and urban districts. The study includes the relation of the weight of the suprarenal to body length, body weight, age, sex, pigmentation, health, vocation and various organs (heart, blood vessels, brain, testes, thyroid, pancreas, spleen, liver, kidneys, and thymus). The following facts are illustrated by two curves and twenty tables. Although there appears to be no specific relation between the weight of the suprarenals and general health or nutritional condition, the average weight of the suprarenals for the war material (423 cases) was 14.9 gm. as compared with 11.7 gm. for normal or control material (480 adult male civilians). The average weight with both sexes together of 613 civilian adults is given as 11.1 gm. The great postnatal loss commences to be regained after 6 months and birth weight is regained by the 12th to 13th year. After 20 years the weight is constant. Sex differences vary with age. Up to puberty the male is slightly larger. Between 16 and 20 years the female adrenals increase greatly over the male. After 30 years the male adrenals are again somewhat the larger. Average adult civilian weight for females is 10.6 (133 cases), for males, 11.7 gm. (480 cases). The specific gravity for the adult is 1038; in premature infants it is higher, in full-term infants, lower; it increases distinctly during the first 6 months of life, then more slowly, remaining lower after the 5th year than it was before this time. In old age the specific gravity again drops. No quantitative relation-
ma). Valle (A.), Siglo méd. (Madrid), 1922, 69, 140-142 (February).

work done by the individual. While there is no correlation of body weight with adrenal weight in the adult, there is a distinct increase in the adrenal weight with increasing stature. The thymus and the testes show a striking parallel increase in weight with an increase in the adult adrenal. The relation in weight of the liver, heart, kidney and pancreas with adrenal weight is not so close. There is no relationship between thyroid weight and adrenal weight. Thirty-two references are given.—A. T. R.

Influence of glands with internal secretion on the respiratory exchange. IV. Effect of SUPRARENAL insufficiency in cats. Scott (W. J. M.), J. Exper. M. (Balt.), 1922, 36, 199-217.

Marine and Baumann have demonstrated a significant and sustained increase in heat production in the majority of rabbits following epinephrectomy. Since the rabbit has relatively great normal temperature variations and usually has accessory suprarenal masses, the author has used the cat for similar experiments because it presents fewer variables. Instead of complete epinephrectomy, partial extirpation, vessel ligation, freezing and various combinations of these methods were used on 35 animals. After preliminary periods on a standard diet, during which time the animals were trained to go into the respiratory chamber without fright, basal metabolism was measured several times. Reduction in the amount of functioning suprarenal tissue was then produced, after which the metabolic measurements were again obtained. Suprarenal insufficiency (cortical injury) produces a picture resembling Graves' disease. A significant and prolonged increase in heat production follows such injury if sublethal. Lethal injury causes lowering of heat production.—I. M.

(ADRENALS) The function of the chromaphil tissue in relation to splanchnic stimulation. Sheen (A. W.) & Vincent (S.), Brit. M. J. (Lond.), 1922, i, 343.

These authors report a series of experiments on cats, with the following results. Peripheral stimulation in cats produces a characteristic curve in which the initial rise is followed by a marked "dip" and a prolonged secondary rise. Elimination of the adrenals from the circulation abolishes or reduces the "dip," the more usual effect of splanchnic stimulation being a simple prolonged rise. While the adrenal elimination is probably an important factor in altering the curve, further experiments are required to determine completely the origin of the "dip." Since some "dip" may occur after the elimination of the adrenals a part of the effect may be normally due to influences other than chromaphil secretion.—F. C. P.

that this finding, if not of diagnostic, is at least of clinical importance.—G. V.

veneno del corazon y de los musculos y las acciones antitoxicas de la adrenalina, de la colestestina y de la glucosa) *Diabetes and to* diabetes is reviewed.—I. M.

DIABETES and bismuth treatment (Diabète et traitement bismuthé).

Bory (L.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1232-1238.

A patient with diabetes of 16 years standing was cured by bismuth. The Wassermann test was negative. *Navarro Blasco*

Influence of glucose on the effects of ADRENALIN on the heart

(Influence du glucose sur les effets de l'adrénaline sur la coeur isolé du lapin). Claes (Mlle. E.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 783-785.

The presence of an extra quantity of glucose in the Locke's solution used for perfusing the rabbit heart is favorable to cardiac work, and permits a prolongation of the stimulating action of adrenalin. Thus, when the amount of glucose in the solution is increased four-fold or more there is considerable increase in the rate and strength of beat, and the addition of adrenalin to the solution with the larger sugar content evokes a notably prolonged excitation.

—W. B. C.

Treatment of the vomiting of pregnancy by ADRENALIN (Tratamiento de los vomitos de las embarazadas por la adrenalina).

Navarro Blasco (F.), Méd. ibera (Madrid), 1921, No. 204, 271-273.

The pathogenesis of vomiting of pregnancy is diversely interpreted by different authors. The theories most credited ultimately refer to the ovaries (Boissard), the corpus luteum (Pinard and Chiril), or the adrenal (Silvestri). The adrenal theory has much in its favor and the excellent results which follow the administration of total suprarenal extract, seems to confirm the etiologic importance of adrenal insufficiency. The author claims to have secured very good results with adrenalin and maintains that all pregnant women who suffer from vomiting ought to be given adrenalin even if in previous pregnancies there has been abortion without the use of this remedy.—E. B.

(ADRENIN) Quantitative test for epinephrin. Okamoto (K.),

Kitasato Arch. Exper. Med. (Tokyo), 1922, 5, 79.

Okamoto has modified the excellent method devised by Suto and Inouye for quantitative estimation with mercuric chlorid of the epinephrin in the blood. Nearly 100% of the epinephrin could be recovered from rabbit and horse blood with this improved method, using only 1 cc. of blood or more.—J. Am. M. Ass., 79, 1729.

ADRENIN cure of polyn neuritis (Polineuritis curada con la adrenalina). Valle (A.), Siglo méd. (Madrid), 1922, 69, 140-142 (February).

work done by the individual. While there is no correlation of body weight with adrenal weight in the adult, there is a distinct increase in the adrenal weight with increasing stature. The thymus and the testes show a striking parallel increase in weight with an increase in the adult adrenal. The relation in weight of the liver, heart, kidney and pancreas with adrenal weight is not so close. There is no relationship between thyroid weight and adrenal weight. Thirty-two references are given.—A. T. R. (W. I.), *J. Industrial Hyg.*, 1922, 3, 610-611.

Van Wagenen carried out this test on a group of fifty students of physical education, of whom he says "a more physically fit, more symptomless group could not have been desired." Reactions were positive in 20% of the cases. A positive reaction consists of an increase in pulse rate and blood pressure of over fifteen points and general symptoms as muscular tremors, weakness, palpitation of the heart, lacrymation, bladder urgency, etc. The type of curve for blood pressure change is the same in positive and negative cases, but differs in quantity only. The 20% of positive reactions "make it seem unlikely that the test can always be relied upon in cases where clinical observation is unable to establish a diagnosis of hyperthyroidism."—Author's Abst.

(AUTONOMIC NERVOUS SYST.) The gastro-intestinal expression of sympathetico- and vago-tonia. Fitts (J. B.), *South. M. J. (Birmingham)*, 1922, 15, 705-708.

This is a discussion of the conditions named in the title on the basis of innervation, followed by 9 brief case reports. Of no direct endocrine interest.—J. C. D.

Experimental studies in DIABETES. The Internal PANCREATIC function in relation to body mass and metabolism. The influence of the THYROID upon diabetes. Allen (F. M.), *J. Metab. Research (Morristown)*, 1922, 1, 619-665.

Since thyroid overactivity tends to lessen carbohydrate tolerance, the idea has persisted in the minds of many that there is some relationship between thyroid and internal pancreatic function. The present work was undertaken to study the possibility of such relationship. The work was done on dogs exclusively. The effects of thyroid feeding and of thyroidectomy in partially depancreatized animals were investigated. It was found that excess thyroid activity in diabetes aggravated the diabetes. No evidence was obtained, however, that diabetes might be caused by overactivity of the thyroid function. In diabetes of moderate severity, deficiency in thyroid function lowered the hyperglycemia and glycosuria, due to the resulting injury and cachexia, but no evidence was available that the severity of the diabetes was thereby lessened or that the change was beneficial. It is concluded that there is no definite antagonism

between the functions of the thyroid and pancreas. The literature on the relation of the thyroid to carbohydrate metabolism and to diabetes is reviewed.—I. M.

DIABETES and bismuth treatment (Diabète et traitement bismuthé).

Bory (L.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1232-1238.

A patient with diabetes of 16 years standing was cured by bismuth. The Wassermann test was positive. Novarsenobenzol was badly tolerated. Benzoate of mercury was also given. The diabetic condition was ameliorated by the anti-syphilitic treatment, which, however, did not obliterate the positive Wassermann reaction. Bismuth preparations (trepol and muthanol) were given twice a week for 5 weeks in 0.2 and 0.3 gm. quantities. The glucosuria disappeared.—F. S. H.

Case of DIABETES MELLITUS with pluriglandular lesions (Un cas de diabète sucré avec lésions pluriglandulaires). Claude (H.) & Schaeffer (H.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1326-1335.

A typical complete case report. Autopsy showed small pancreas and adrenals. The thyroid appeared normal. A diminution in the number of islets of Langerhans and general microscopic atrophy of the pancreas was noted. The cortical cells of the adrenals were small. The thyroid was normal. The hypophysis was markedly atrophied. The case was complicated by pulmonary tuberculosis. Nephritis was also present.—F. S. H.

(DIABETES) Further observations on the nature of the reducing substance of human blood. Cooper (E. A.) & Walker (H.), Biochem. J. (Lond.), 1922, 16, 455-459.

A theory of the causation of diabetes is advanced which is based on the hypothetical inability of the organism to convert glucose into the reactive ethylene oxide form.—F. S. H.

The presence of aldol in DIABETIC urine (Ueber die Auffindung von Aldol im Diabetikerharn. Fricke (R.), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1922, 118, 218-223.

Small amounts of aldol were demonstrated in urine from diabetics.—F. S. H.

The immediate influence of alcohol ingestion upon DIABETIC glycosuria and blood sugar. Fuller (L. S.), J. Metab. Research (Morristown), 1922, 1, 609-618.

The object of the experiments reported in this paper was to determine the immediate effect of alcohol on hyperglycemia and glycosuria of diabetics. It has been known that alcohol, when used

to raise the total metabolism above the caloric tolerance of a diabetic patient, causes hyperglycemia and glycosuria, but that it tends to reduce the formation of ketone substances. In the present research alcohol was added to standard diets and given to diabetic patients of varying degrees of severity. The plasma sugar, urine sugar and total ammonia and nitrogen output was determined. It was found that alcohol ingestion lowered glycosuria and hyperglycemia significantly in the mild and moderately severe cases, but caused only light diminution in the very severe cases.—I. M.

— The fat content of the blood and liver and the glycogen content of the liver in **DIABETIC** coma (Über den Gehalt des Blutes an Fett und über den Gehalt der Leber an Fett und Glykogen im diabetischen Koma). Geelmuyden (H. C.), *Acta Med. Scand.* (Stockholm), 1920, 53, 381-392.

The author has studied 10 cases of diabetes mellitus and 4 cases of various diseases. The fat content of the liver was tested by Kumagava-Suto's method, and of the blood by Shimidzu's method. The glycogen of the liver was tested by the method of Pflüger. The autopsies were sometimes made as late as 48 hours after death. The author found the fat considerably increased in the blood, but not in the liver; the latter held glycogen, sometimes in great amounts. He discusses the relation between experimental diabetes in dogs and diabetes mellitus of men and concludes that they are the same in principle, and that the differences are due to differences in the rapidity of the development of the pathological changes.

—H. B.

Divided meals for severe DIABETICS. Gray (H.), *Boston M. & S. J.*, 1922, 186, 763-768.

The author reviews the evidence which suggested that this treatment would be useful and reports 4 cases thus treated from Dr. E. P. Joslin's clinic, where the idea originated. (See also Dr. Murayama's case abstracted in this number.) The treatment is based on the observation that if a heavy meal is preceded by a light meal of carbohydrates, more food can be taken at this second meal without dangerous results than if there were no preceding or "activating" meal. Six meals a day are given. A meal of fruit (orange or grapefruit) precedes each of the heavy meals by one to two and one-half hours. Breakfast is the lightest of the heavy meals. The other heavy meals are each of about the same value.—J. C. D.

On the basis of the development of the DIABETES and the chief types of that disease (with a few remarks as to certain changes of the PANCREAS in dogs). Heiberg (K. A.), *Acta Med. Scand.* (Stockholm), 1917, 50, 663-670.

Two types of primary diabetes may be distinguished: cases with the damage limited to the pancreas islands, and other cases. In the

cases of the first group the islands are more or less decreased in number and the undestroyed islands show granular degeneration and other pathological changes. In the other cases in which the remaining glandular tissue is also affected a low number of islands may also be found. In the remaining islands there are often connective tissue and hyalin changes. Galloping diabetes may be identified with the affection of the pancreas islands solely. The author points out that in Allen's experimental diabetes the anatomical changes are different from those in men. There are no grains and no round cells to be found in dogs; the islands are all affected, but none disappears totally. Hence conclusions drawn from comparisons between the conditions of dogs and human beings must be accepted with the greatest caution.—H. B.

Renal DIABETES (Till fraagan om diabetes renalis). Johnsson (A.), Finska Läksällsk. Handl. (Helsingfors), 1922, 64, 429-441.

Two cases of typical renal diabetes are reported. Case 1 was that of a male aged 35 years in whom the condition had existed, without any change, for 10 years. Case 2 was that of a woman, aged 44 years, in whom sugar had been found in the urine for 16 years without any apparent change in the disease. In the latter case the father and all her sisters had suffered from mild diabetes mellitus.

—D. J. G.

Decreasing DIABETIC mortality; increasing incidence of glycosuria. Joslin (E. P.), Boston M. & S. J., 1922, 186, 761-763.

The title covers the subject matter dealt with.—J. C. D.

Prognosis in DIABETES MELLITUS. Lyon (D. M.), Lancet (Lond.), 1922, i, 1043-1045.

The author points out the necessity of making sure that the case is one of diabetes melitus and not merely glycosuria which may have other causes. He advises that prognosis be withheld until the effect of treatment has been ascertained. No new data are presented.—I. M.

Hipertension y DIABETES. Marañón (G.), Arch. de cardiol. y hematol. (Madrid), 1922, 4, 125-131.

The relation between hypertension and diabetes is one of the least known of the many obscure points of this affection. The author has recently studied 90 cases of diabetes which show that this is present in those ages of the individual in which hypertension generally exists. In those of 40 years of age there were 10 cases in which the maximum tension was below 180; 2 between 180 and 210; and above 210 no case. Between 40 and 50 years, 17 cases had pressure below 180; 11 between 180 and 210; and 15 above 210. The systematic determination of the pressure in non-diabetic patients of corresponding ages showed some moderate hypertension. In

healthy men above 40 years of age there was likewise permanent or transitory hypertension, not dependent upon habitual causes (renal sclerosis, vascular affections, etc.). There exists, therefore, a chronological relation between hypertension and diabetes. In many patients hypertension is found before glycosuria and the complete syndrome of diabetes appears. When this latter is established hypertension is present for some years, but later diminishes. In such cases the development of diabetes is characterized by the augmentation of glycemia, diminution of carbohydrate tolerance, intensification of the nervous and circulatory phenomena which follow an injection of adrenalin, and in some cases by the manifestation of certain symptoms which mark the beginning of diabetes. This may be considered a prediabetic state. In 22 cases of hypertension without glycosuria Marañón has encountered hyperglycemia in 14. The cause of the hypertension was different. It is necessary to be extremely careful in the diagnosis of "essential hypertension." In 7 of the 22 cases of hypertension, delayed investigation of the renal function showed the existence of sclerotic renal lesions, constituting evidence favorable to the hypothesis recently sustained by Neubauer, Novoa Santos and others concerning the existence of hyperglycemia in chronic nephritis. In 4 of the 22 cases there was arteriosclerosis of the aorta or peripheral vessels without any renal disturbance. In another series there was no renal or vascular trouble; such cases should be considered provisionally as cases of essential hypertension. Investigation of alimentary glycosuria in 7 cases of this group showed that there was glycosuria in 3 after ingestion of 100 to 150 gm. of glucose. In this state of preglycosuria it is possible to find diabetic symptoms such as eruptions, furunculosis, cataracts, etc. The cause of such appearances is not clear, some authors having attributed them to hyperadrenalism. A permanent state of hypersecretion of the suprarenals could scarcely be the direct and sole cause of a chronic affection such as diabetes with hypertension. The facts indicate, nevertheless, that this endocrine factor intervenes in one group of diabetic cases, described by Falta.—E. B.

The advantage of multiple meals in the treatment of severe DIABETES. Murayama (T.), Boston M. & S. J., 1922, 186, 768-775.

A case report. The essentials of the treatment are given in the abstract of Dr. Gray's article in this number. The patient, a woman of 41, was first seen in 1919. During the ensuing two years she came into the hospital five times, in a worse condition each time. Her final treatment, on the basis of divided meals, was strikingly successful in reducing the sugar in the urine and blood, and in restoring the nitrogen balance. There are full tables of the sugar estimations, etc., as well as a schedule of the meals.—J. C. D.

The etiology and treatment of DIABETES. Renshaw (A.) & Fairbrother (T. H.), Brit. M. J. (Lond.), 1922, i, 674-677.

Not of endocrine interest except that the authors report the isolation, from the stools of diabetic patients, of an organism which produced acetone, diacetic acid, oxybutyric acid, and butyl alcohol. They conclude that these organisms produce the same products in the alimentary canal of man and that their absorption so affects the glycogenic function of the liver as to lead to the improper storage of glucose.—F. C. P.

Biedl's experimental glycosuria and its relation to DIABETES MELLITUS (Om Biedl's experimentalla glykosuri och dess foerhaallande till diabetes mellitus). Savolin (M.), Finska Läksällsk. Handl. (Helsingfors), 1922, 64, 456-482.

The author repeated the experiments reported by Biedl in 1898 by occluding in a number of cats the thoracic duct through a ligature around the left jugular, the left axillary and the anonyma veins and obtained slight glycosuria in some of them. He collected lymph from the thoracic duct and injected it into cats made diabetic by the extirpation of the pancreas, but without any reduction in glycosuria. He concludes that the incretion of the pancreas does not enter the blood via the thoracic duct. He also examined the reports of cases of occlusion of the thoracic duct in the human beings which have been reported in the literature and comes to the conclusion that glycosuria did not result.—D. J. G.

Clinical observations concerning progressiveness of DIABETES. Sherrill (J. W.), J. Metab. Research (Morristown), 1922, 1, 667-721.

It has long been a question in the minds of most people whether diabetes mellitus takes a progressive, downward course in spite of all treatment. The author, after pointing out the necessity of controlling all methods of examination and of having absolutely reliable observations over a considerable period, presents data from 5 severe cases of youthful diabetes with the contention that the disease does not take a progressive, downward course if treatment is followed. It is pointed out that the progressiveness often noted is traceable to definite causes such as dietary excesses and infections particularly and that it may be accounted for by individual variations in susceptibility to such disturbing factors. Avoidance or removal of such factors is said to be sufficient to prevent downward progress.—I. M.

The identification of the substance in urine of DIABETICS which reacts as acetaldehyde (Ueber die Identifizierung der aldehydartig reagierenden Substanz im Harn von Diabetikern als Acetaldehyd). Stepp (W.) & Fuelgen (R.), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1921, 114, 301-306.

Types of DIABETES MELLITUS. Wilder (R. M.), Med. Clin. N. Am. (Phila.), 1921, 5, 455-467.

There is still some confusion in the classification of the types of diabetes mellitus, and even with an accepted classification, a certain degree of overlapping is unavoidable. Despite this difficulty, certain very definite clinical features permit a grouping of cases into the following types which the author, in a series of 298 patients observed in the Mayo clinic, has found advantageous. Group 1 consists of acute diabetes (constituting 19% of the series), characterized especially by abrupt onset and gradually failing carbohydrate tolerance, strength and weight; group 2, vascular diabetes, associated with hypertension or arterio-sclerosis or both, with or without renal complications; group 3, diabetes of obesity, characterized by obesity, without evidence of vascular disease; group 4, interstitial pancreatitis; and group 5, miscellaneous persistent glycosurias. A differentiation of these several types of diabetes is of more than mere academic interest. The prognosis in a given case depends more on the nature of the underlying diabetes than on the temporary severity of the cardinal symptoms or the intensity of the glycosuria. Surgical risks are also to be evaluated according to the existing type of diabetes.—I. B.

Sudden death from cardiac failure in DIABETES MELLITUS.

Williamson (R. T.), Practitioner (Lond.), 1922, 109, 279-282.

The title covers the entire subject matter of the article, which is not of immediate endocrine interest.—J. C. D.

The use of neuccesol in DIABETES INSIPIDUS (Über die Anwendung des Neuccesols beim Diabetes insipidus). Deloch (E.), Therap. d. Gegenw. (Berl. u. Wien.), 1921, 62, 363-364.

Though the use of posterior pituitary is recognized as the best known means of alleviating the symptoms of diabetes insipidus, the fact that it must be hypodermatically administered by the physician renders its use expensive to persons of moderate means. Moreover, the relief obtained from this substance is transient. With the hope of finding a substance which may be employed by mouth, Deloch tried cesol, a derivative of pyridin, and neuccesol (Merck), obtained from the reduction of cesol. Neuccesol resembles pilocarpin in physiological effects, although it is not so potent except in patients with an unstable nervous system. From a study of three patients with diabetes insipidus, the author arrives at the following conclusions. Cesol and neuccesol exert no material influence on the urine and blood. There is no material influence upon the gastrointestinal symptoms. To a certain degree there is a favorable influence upon the thirst and the dryness in the throat, inasmuch as there occurs an increase in salivary secretion. Mild diaphoresis occurs, which is agreeable to the patient. Subcutaneous injections of these substances yield better results than their administration in tablet form by mouth.—I. B.

Cure of DIABETES INSIPIDUS with novarsenobenzol (Diabète insipide guéri par la novarsénobenzol). Labbé (M.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1230-1232.

Report of a patient giving history of cranial injury in the war and, later, malaria. Thirst and polyuria of 3 to 4 liters a day was manifest. Urine was normal. There was vertigo, mild nystagmus and neuralgia. The Wassermann test was negative in both the blood and cerebro-spinal fluid. The sella turcica was malformed. Treatment with pituitary extract gave no relief. The administration of novarsenobenzol in an initial dosage of 0.15 gm. increased to 0.30 gm. for 4 days reduced the urine output to 1500 cc.—F. S. H.

The differential diagnosis of polyuria, with special reference to DIABETES INSIPIDUS. Rowntree (L. G.), Med. Clin. N. Am. (Phila.), 1921, 5, 439-453.

A general discussion of the various types of polyuria. A review of the literature, including the 34 cases of the 370,000 records of patients of the Mayo clinic, reveals the fact that diabetes insipidus is a rare condition, there having occurred but 113 cases in a total of 800,000 patients. A case of primary diabetes insipidus is cited in an unmarried woman of 34, in whom the urinary output of over 12 liters a day was reduced to from 2 to 3 liters daily through the subcutaneous injection of the extract of 1 cc. posterior pituitary gland four times a week. Such measures as spinal puncture, the ingestion of fresh posterior pituitary (up to 18 fresh glands daily), the administration of histamin, valerian, ergot, diuretin, pilocarpin, and atropin, and the administration of pituitary extract with Lloyd's reagent and salol coated pills were all tried and failed to relieve the patient. In the consideration of diabetes insipidus, the following conditions must be borne in mind for the purpose of differential diagnosis: physiologic polyuria, diabetes mellitus, chronic interstitial nephritis, polycystic disease of the kidneys, infection of the kidney or of the urinary tract, and functional nervous disorders. It must be remembered that cases are on record in which diabetes insipidus has terminated in diabetes mellitus.—I. B.

ENDOCRONOLOGIA y tuberculosis. Alou (P.), Union méd. (Zaragoza), 1922, No. 222, 301-305.

In tuberculosis the organism is a factor of more importance than the microbic factor. Clinically considered, tuberculosis is more hereditary than contagious, since tuberculous infection attacks an organism in which some toxic cause alters the organic endocrine tone and thus produces suprarenal hyperfunction.—E. B.

The influence of the ENDOCRINE GLANDS on the secretion of gastric juice. Alpern (D. E.), Vrachebnoié Délo (Kharkov), 1922, 5, No. 10-12; abst., Presse méd. (Par.), 1922, 30, 795.

Alpern's investigations have been carried out on dogs operated upon according to the method of I. Pavlov, in the laboratory of general and experimental pathology at the Veterinary Institute of Kharkov. Intravenous injections of adrenin, given in doses sufficient to cause typical modification of arterial pressure, does not exercise an appreciable influence on the first phase of gastric secretion; that it is momentarily retarded is explained by the vasoconstrictor effect of adrenin, especially since this effect is particularly marked upon the arteries of the abdominal organs. Intravenous injections (1 to 10 solutions) of extract of the intermediate lobe of the hypophysis (in doses of 0.025 gm. to 0.075 gm. per kg. body weight) exercises a marked depressing effect, which persists 2 or 3 days after the injection. The acidity and the digestive power of the gastric juice are generally decreased, but it is particularly the quantity of the secretion which is modified. In order better to judge the intensity of this action on gastric secretion, the author gave subcutaneous injections of pilocarpin 0.005 gm. per kg. body weight. This caused increase of gastric secretion from 25 to 40 cc. in 5 minutes. It was then shown that an intravenous injection of hypophyseal extract (intermediate lobe) is given simultaneously with pilocarpin, the secretion is stopped for the first 5 minutes; then it begins again, but with an output of 2 to 5 cc. per 5 minutes.

—R. G. H.

(ENDOCRINE) El metabolismo basal en la clinica. Alvarez (A. C.), Arch. de med., cirug. y espec. (Madrid), 1922, 9, 5-32.

A general review of the literature and evaluation of the significance of basal metabolism.—R. G. H.

(INTERNAL SECRETION) Bibliography on constitution for 1920 (Bibliographie auf dem Gebiete der Konstitutionslehre in Jahre 1920). Bauer (J.), Ztschr. f. Konstit. (Berl.), 1922, 8, 420-458.

Over 800 titles are listed under a general heading and eight systems of organs, there being about 200 references on internal secretion.

(ENDOCRINE) Scleroderma en plagues. Arzt, Wien. klin. Wchnschr., 1922, 35, 680.

Not of endocrine interest.—J. K.

(ENDOCRINE ORGANS) The condition of the body in the long-lived (Studien zur Körperverfassung der Langlebigen). Boening (H.), Ztschr. f. Konstit. (Berl.), 1922, 8, 459-506.

The organ weights and incidence of certain pathological conditions are given for 50 men and 50 women from 80 to 96 years of age and compared with similar data for the ages 60 to 64 years and 70 to 74 years. The weight of the thyroid gland and the incidence

of goiter was higher in the oldest group. The suprarenals showed some senile atrophy. There was a much larger percentage of hyperplastic change in the female than in the male suprarenal. The weight changes in the testes were negligible, but there was a distinct increase in the percentage of hydrocele and healed periorchitis in the very old. The prostate showed marked enlargement with old age. The ovaries and spleen showed atrophy, especially the spleen of the female. Some literature is given.—A. T. R.

INTERNAL SECRETIONS and the home. Bond (E. J.), *Ment. Hygiene* (N. Y.), 1922, 6, 522-525.

A satirical portrayal of some of the "modern" trends in the field of endocrinology whereby all social and domestic troubles are solved, and an endocrine utopia outlined.—Frederick H. Allen.

(ENDOCRINE) El metabolismo basal. Bonilla, *Méd. ibera* (Madrid), 1921, 14, 478-479.

An extensive discussion of the basal metabolism determinations in the diagnosis of endocrine diseases.—G. M.

(ENDOCRINE) Biochemical research in normal and in frightened animals (*Ricerche biochimiche in animali normali ed in animali emozionati*). Buscaino (V. M.), *Riv. di patol. nerv.* (Firenze), 1919, 24, 11-12.

For data, see *Endocrin.*, 6, 270-271.—G. V.

(ENDOCRINE) Progressive lipodystrophy in a 40 year old man (*Lipodystrophie progressive chez un homme de 40 ans*). Christiansen (V.), *Rev. neurol.* (Par.), 1922, 29, 1169-1175.

Report of a case of lipodystrophy in a man of 40 years. The distribution of the emaciation was modified by the secondary sex characteristics.—C. E. N.

Sympathique et glandes ENDOCRINES. Claude (H.) & Piédelièvre (R.), *J. méd. franç.* (Par.), 1921, 10, 223-227.

(ENDOCRINE) Acrocephalia-syndactylia: congenital dysendocrinism (*Acrocefalo-sindattilia, contributo allo studio delle disendocrinia congenite*). Coppola (A.), *Riv. di patol. nerv.* (Firenze), 1919, 24, 283-339 (December).

Report of a case of acrocephalia-syndactylia in a man 59 years old. The Wassermann test confirmed congenital syphilis as an etiologic factor. Besides characteristic symptoms of the malformation there was a persistent thymus, hypothyroidism and radioscopy of the hypophysis, while revealing a shortened antero-posterior diameter of the cranial base, showed a very irregular sella. The anterior clinoids were very evident; the floor of the sella, with an

opening of 16 mm., was flat oblique, downward and backward, without any sign of lamina quadrilatera or of posterior clinoids, and downward a triangular shadow, almost vertical, like a persistent cranio-pharyngeal canal, could be seen. There was palatoschisis and eight upper and eight lower teeth, the upper median incisors being posterior to the tooth line. There was strong ortostatic tachycardia (26 more pulsations). The oculo-cardiac reflex was inverted and there was greater pulse rate while the patient was asleep. He had polyuria, anhydrosis and a great tendency to fall asleep as soon as put into a horizontal position. Hypotricosis, except in the head, was manifest. There were fat deposits under the clavicles and on the mons veneris and a decided functional hypogenitalism in spite of apparently well developed external genitalia; the testes, however, were very soft. Th author believes that these disorders were caused by the influence of the syphilis on the hypophysis, upon which all disorders of growth probably depend, as well as the consequent pluriglandular dystrophy.—G. V.

The psychic problem from the ENDOCRINE standpoint (Nagra endocrina synpunkter rörande själsproblemet). Hammar (J. A.), Upsala Läkaref. Förh., 1921, 26, 177-204.

A review of the known relations between the psyche and the endocrine glands. The "psyche" is only an abstraction just as, for instance, the idea of "sickness" is an abstraction. The psychic processes are based on the chemical reactivity of the nervous element. Having exemplified endocrine influences on the psyche the author claims that hormones like bacterial toxins and other poisons have an elective affinity. A comparison of the clinical symptoms and the anatomical changes of the brain in cases of poisoning will perhaps at some future time give some knowledge of the localization of the psychic functions. "Nervousness" may be due to an abnormal affinity, hereditary or acquired, to certain materials. It is possible that the same hormone that gives a certain habitus has an influence on the psyche; and hence we have more right to judge of the mind from the exterior than is nowadays recognized. On the other side, the psychic processes most probably exert some influence on the secretion of the hormones, just as they have an influence on the secretions of the stomach. The outer somatic phenomena of the emotions may be mediated in this way. A condition of chronic irritability of certain organs may be the product of strong and lasting emotions. That we are not able to distinguish the psychical phenomena which are due to endocrine changes is due to the insensibility of the endocrine glands. The different conditions of the same brain may be explained perhaps by the changes of the endocrine system.—H. B.

(ENDOCRINE) Les Lipoides. Iscovesco (H.), Presse méd. (Par.), 1922, 30, 653-655.

Although the term "lipoids" is commonly used to designate the whole group, adepoids should be used, retaining the term lipoids for certain derivatives only. Adepoids are products of initial extraction of tissues by ether, chloroform, benzol and allied solvents, but they contain many impurities. From them, true lipoids may be isolated in pure form, which, although fat-like in appearance, are no more "fats" than vaseline. The adepoid molecules are far larger than those of the true fats; the latter contain but three elements (CHO); the adepoids contain at least four (CHON), but mostly five elements (CHONP). The adepoids are composed of one or more fatty acid radicals, with one or several nitrogen bases (which determine the characteristic properties of a given lipid). Cholesterol is an adepoid, not a lipid; but it always accompanies lipoids and seems to have a stabilizing or neutralizing influence which either restricts or compensates the activities of the lipoids. Lipoids, isolated in pure form, were used in all of Iscovesco's experiments. Lipoids are no more colloids than ferrous hydroxide, for example, but they may appear in colloid suspension and form fine emulsions with water. Overton's conception that lipoids controlled all cell metabolism is untenable today; lipoids play a dominant part only in certain processes, narcosis for example. In immunity the activities of the lipoids are determined by the physico-chemical properties of such lipoids as happen to be present in a given case; there is probably no fundamental law governing immunity reactions, just as there is no common law for the metabolism of inorganic salts in the body; yet salts as well as lipoids are essential to health. Lipoids are indispensable for life and growth. According to Iscovesco, malnutrition is merely lipid starvation; the value of cod liver oil in diseases of malnutrition (keratomalacia, osteomalacia, rickets) was demonstrated by him to be due to the hepatic lipoids which it contains; removal of these lipoids robs the oil of its therapeutic effect. The work of Iscovesco and many others furnishes evidence of the specific action of the lipoids obtained from divers tissues (heart, ovary, brain, placenta, corpus luteum, blood corpuscles, thyroid, suprarenal cortex or medulla); it has also revealed that certain lipoids have a specific affinity for certain organs. Lecithin administered by mouth is not disintegrated by the lipolytic ferments of the digestive tract, and is retained by the liver and the muscles, but not by the brain (Franchini); whereas Frankel's sahidine, a constituent of cephaline, when fed by mouth, causes a marked increase of the phosphorus-lipoid content of the brain (Salkowski). The value of the therapeutic administration of lipoids has been proved conclusively: a case of untractable acne, due to ovarian hypofunction, has been cured recently by the use of the ovarian lipid; the hepatic lipid is being used in preference to cod liver oil, with better and quicker results for infants and for incipient tuberculosis in adults; the cardiac lipid is the most effective and the most harmless of

cardio-stimulants. Iscovesco believes that physiologists and physicians would meet on common ground if they would realize that opotherapy is nothing but "homo-alimentation": the furnishing ready-made to the organism such substances as it has lost the power to synthesize; the theory of homo-alimentation is vindicated by the selective affinity of certain lipoids for certain organs. If the lipoid-soluble A vitamine exists, which he doubts, it will be found chiefly in the lipoids of liver and pancreas. The specific action of the lipoids is likely to found the result of the nitrogen base which a given lipid contains.—G. L.

ENDOCRINOLOGY and psychology. The **ENDOCRINE SYMPATHETIC** system in the modern analysis of human personality (*Endocrinologia e psicologia. II. Sistema endocrino-simpatico nell' analisi moderna della personalità umana*). Pende (N.), *Quaderni di psichiat.* (Genova), 1921, 8, 121-136.

In this monograph a classification of different temperaments is attempted on the basis of the predominance of this or that endocrine gland.—G. V.

(INTERNAL SECRETIONS) The law of morphogenic correlation of Viola and the basis of the pathology of growth and constitution (*Das Gesetz der morphogenetischen Korrelation von Viola und die Grundlagen der Pathologie des Wachstums und der Konstitution*). Pende (N.), *Ztschr. f. Konstit.* (Berl.), 1922, 8, 378-403.

A restatement of the views of Viola and his pupils on the independence and antagonism of development between the vegetative and somatic systems and the predominance of the one or the other system in the two opposite types of man. This principle together with the principle of alternating phases of growth of different portions of the body (as supported by Godin) and that of the existence of two antagonistic groups of hormones (one stimulating growth of mass and development of the vegetative organs and the other producing morphological development and growth of the somatic system) are considered principles without which one can understand neither the physiology and pathology of growth nor the determination of individual human constitution. They are regarded as principles which make it possible to correct many defects by the application of rational nutrition, physical therapy, endocrinotherapy, etc. A list of references to the related work of Viola and his pupils is given.—A. T. R.

ENDOCRINE imbalance and mental deficiency. Potter (H. W.), *J. Nerv. & Ment. Dis.* (N. Y.), 1922, 56, 334-345.

In a survey of endocrine disorders, 849 patients were examined in the feeble-minded institute of Letchworth Village. Of the total, 37% showed definite signs and characteristics which may be con-

sidered as pointing to an endocrine imbalance. Each one of these patients presented a definite symptom complex. There were two distinct age periods in which the greater number of cases were found; the first between the ages of 12 and 16 was contributed to largely by the status lymphaticus group, and the second, over the age of 20, contained groups characterized by disorders of the pituitary body and thyroid gland.—C. E. N.

(ENDOCRINE) A new form of glycosuria (*Sur une nouvelle forme de glycosurie chez les grenouilles*). Przyleski (J.), Arch. internat. de physiol. (Par.), 1922, 19, 143-145.

Frogs abruptly changed from a temperature of 0° to 20° or 25° C., whether kept in water or in a moist chamber, have a glycosuria not present at the lower temperature. It lasts for 24 and even 48 hours, is rarely present after 60 hours, and is absent after 72 hours. Change from 0° to 10° produces no effect. The glycosuria is the result of hyperglycemia.—W. B. C.

(ENDOCRINE) Clinical observations with Benedict's new portable respiration apparatus. Roth (P.), Boston M. & S. J., 1921, 184, 222-230.

Suggestions and information are offered relative to technic, calculations, standards and bibliography.—H. W.

ENDOCRINE insufficiency and chronic intestinal disease. Sadler (F. J.), Lancet (Lond.), 1922, i, 929-931.

The author describes briefly a heterogeneous group of indefinite old age ailments, such as neurasthenia of the climacteric in women, arterio-sclerosis, thyroid deficiency edemas, etc., in which he empirically employed thyroid extract with good results. Nothing new or definite is presented.—I. M.

The influence of the INTERNAL SECRETIONS on the nervous system. Schafer (E. S.), J. Ment. Sc. (Lond.), 1922 (October). Reprint, 21 p.

A general discussion leading to the conclusion that a great deal is already known regarding the influence of the incretions upon the nervous system, but that much more remains yet to be discovered —R. G. H.

(ENDOCRINE) Hyperglycemia in a series of cases showing anxiety, fear, apprehension, etc. Schwab (S. I.) & Jones (A. B.), J. Missouri M. Ass. (St. Louis), 1921, 18, 182.

(ENDOCRINE) Opothrapy in dermatoses (*Opoterapia de procesos dermosifilograficos*). Sicillia, Ann. Acad. de méd. chir. españ. (Madrid), 1922, 66-69; Méd. iberica (Madrid), 1921, 15, 500.

Many affections of the skin, among them psoriasis, are of endocrine origin (thyroid, hypophyseal, suprarenal, genital, etc.). Endocrine psoriasis is characterized by the predominance of erythema with colorations very much accentuated by the chronicity of the process, by its beginning in distinct situations, and by the non-peeling character of the skin. Many forms of baldness are also of an endocrine nature, as well as some of the dermatoses of the menopause and of puberty, due to ovarian insufficiency.—E. B.

(GONADS) Ovarian insufficiency and abortion (*La insuficiencia ovarica como causa de aborto*). de Andres (V.), Clin. Castellana (Valladolid), 1921, 621-627 (Oct.).

Clinical history of a patient exhibiting evident symptoms of ovarian insufficiency and who as a primipara suffered abortion without apparent cause. Upon becoming pregnant a second time she was submitted to ovarian opotherapy, following which the pregnancy progressed normally until the medication was suspended. Four days later a second abortion occurred. A third pregnancy took place and during the whole period of gestation she was treated energetically by like medication. Normal childbirth occurred. The author presents this case as proof that insufficiency of the ovary may be the direct cause of abortion.—E. B.

(GONADS) Sur le développement des caractères sexuels primaires chez les Urodèles. Hypothèse sur son déterminisme. Aron (M.), Compt. rend. Acad. d. sc. (Par.), 1922, 174, 1568-1570.

Reference from Ber. ü. d. ges. Physiol., 14, 475.

(GONADS) Transplantations testiculaires seminifères et interstitielles. Bolognesi (G.), J. d'ûrol., 1921, 12, 153-173.

After removal of vas deferens and epididymis, atrophy of the seminiferous tubules takes place, but hypertrophy of the interstitial cells. On transplanting a testis so treated to another animal no change was observed in the sexual activity or general condition, the transplant degenerating into ordinary connective tissue. Hence it is concluded that the internal secretion of the testis is not derived from the interstitial tissue.—Physiol. Abst., 7, 373.

(GONADS) Three cases of hermaphroditism (*A propos de trois observations d'hermaphroditisme*). Chaton, Bull. Soc. d'obst. et de gynec. de Par., 1922, 11, 506-510.

The first case was that of a soldier of 22 years in whom a uterus was found at operation for hernia. Psychically the individual was male. Spermatozooids were found in the testes. The second case was that of a "woman" of 59 having both a small penis and vaginal orifice. The third case was that of a girl of 8 years with external female genitalia and intraabdominal testes. She was psychically a female.—F. S. H.

(OVARY) The metrorrhagias of young girls (Contribution à l'étude des metrorragies chez la jeune fille). Couinard (F.), Thèse de Paris, 1921; abst., *Rev. franç. de gynéc. et d'obst. (Par.)*, 1922, 5, 318 (May).

A discussion of the anatomic causes of metrorrhagia in girls, with only incidental mention of the rôle of the ovary. The author emphasizes the frequency of polycystic ovaries in the causation of this disorder. Treatment is most often purely medical or radio-therapeutic.—E. N.

(GONADS) A histological study of the undescended TESTICLE of the horse. Crew (F. A. E.), *J. Comp. Path. & Therap. (Edinb.)*, 1922, 35, 62-69.

Reference from *Ben. d. d. ges. Physiol.*, 14, 206

(GONADS) DYSOVAIRE. Palché (P.), *Gynéc. (Par.)*, 1922, 21, 449-452.

Glandular interdependence necessitates consideration of pluri-glandular treatment of dysovarianism. With this in mind Palché reviews the various reports of the use of ovarian, mammary, thyroid, adrenal and pituitary preparations in disordered ovarian function. The details of the article are not susceptible to brief abstracting.

—F. S. H.

(GONADS) Transplantation of OVARIAN tissue (Contribution à l'étude de la greffe clinique de tissu ovarique). De Bruyne (F.), *Soc. belge de gynéc. et d'obst.*, 1922 (May); abst., *Rev. franç. de gynéc. et d'obst. (Par.)*, 1922, 17, 447 (Aug.).

A histological study of ovarian tissue which had been grafted in the subcutaneous tissue of the abdominal wall 173 days previously in a patient of 25, who had at that time undergone subtotal hysterectomy and bilateral ovariectomy for adnexal tumor. The grafts were removed because of swelling, pain, and tenderness. The removal was followed by the appearance of menopausal symptoms, which previously had been absent. The grafts were found to consist of cysts in a cicatricial tissue. The cyst walls showed three layers. The outer was dense and fibrous. The middle was made up of large oval cells with central spherical nuclei, and large vacuoles in the protoplasm, surrounded by a little connective tissue with numerous vessels. The innermost layer was made up of lutein cells. A comparison of these with the lutein cells of a normal corpus luteum and those of polycystic lutein degeneration, led the author to conclude that this tissue was quite different, and was perhaps due to abnormal proliferation. Statistics of the Gand clinic show that in cases in which the graft is hypertrophied post-operative menopausal symptoms are less frequent than when there has been no transplantation or when the graft does not exceed the size of a pea.

Fragments of transplanted corpus luteum hypertrophy in not over 20% of the cases, of the medullary zone in 33%, of the cortical zone in from 70% to 100%. It is also this last named portion which seems to protect against symptoms of insufficiency.

(GONADS) Emotional metrorrhagia (*Les métrorragies émotives*).

Fabre (M.), Thèse de Paris, 1921; abst., *Rev. franç. de gynéc. et d'obst.* (Par.), 1922, 5, 319 (May).

Strong emotion, such as anger or fear, may cause profuse uterine hemorrhage. The same is true of less violent emotions, frequently repeated. The occurrence is most often noted at the approach of menstruation, when utero-ovarian activity is at its maximum. These hemorrhages the author explains as due either to the effect of the emotion upon the uterine vaso-motor centre (vaso-dilator excitation, with vaso-constrictor inhibition) or to an effect upon the ovary itself (hyperovarism).—E. N.

(GONADS) Solid tumors of the OVARY and pregnancy (*Tumeurs solides de l'ovaire et grossesse*).

de Fourmestraux (J.), *Arch. méd.-chir. de Province* (Tours), 1921, 11, 267-278.

(GONADS) Seasonal changes in the TESTIS of *Gambusia affinis*, the top minnow. Geiser (S. W.), *Anat. Record* (Phila.), 1922, 23, 104-105.

The article is not of immediate endocrine interest.—W. J. A.

(GONADS) Hermaphroditism and gonochorism in hydra (*Hermaphroditismus und Gonochorismus bei Hydrozoen*).

Goetsch (W.), *Zool. Anz.* (Leipz.), 1922, 54, 6-18.

By grafting part of a male strain of *Hydra attenuata* to a portion of a female strain the author succeeded in one case in getting among the descendants some individuals with testes and others with ovaries, but testes and ovaries never occurred in the same animal. These animals were sterile. He found also intermediate stages between typical hermaphroditism and gonochorism. Eleven references are given.—A. T. R.

(GONADS) Hermaphroditismus und Gonochorismus bei Hydrozoen.

Goetsch (W.), *Zool. Anz.* (Leipz.), 1922, 54, 294-301.

Reference from *Ber. ü. d. ges. Physiol.* (Berl.), 1922, 14, 320 (Oct. 18).

Endocrine aspects of EUNUCHOIDISM (*Conceptos endocrinológicos del tipo Eunucoide*). Goñalons (G. P.), *Prensa méd. Argentina* (Buenos Aires), 1921, 20 Agosto.

The author studied carefully with photograph, skiagram and musical studies of the voice, four men and one woman of eunuchoid

type. He believes that eunuchoidism is the consequence of traumatic or pathological castration in both sexes, realized or verified at the beginning of puberty. The eunuchoid type is represented by subjects of relative high stature, long arms and legs, atrophy of gonads, absence of the mammary glands, and infantile voice.

—G. P. G.

(GONADS) Congestiones oculares en la menopausia. Gonzalez (J.), Méd. iberica (Madrid), 1922, No. 253, 357-359.

At the menopause many manifestations of ocular pathology, such as uveitis, iridocapsulitis, iridocoroiditis and a tendency to glaucoma, cataracts, etc., are seen. The ocular disturbances are sometimes limited to slight diminution of the acuteness of vision. In the menstrual period and a few days prior to the period very intense iritis, congestions of the iris and of the conjunctiva have been observed. The subjects who present more or less intense ocular lesions during the menstrual period are those who suffer lesions of more consequence when they arrive at the critical age than those who sometimes exhibit atrophy of the optic nerves. In these disturbances, especially in those of a congestive type, ovarian opotherapy exercises a favorable influence and largely confirms their pathogenesis.—E. B.

The GONADS of *Rhizostoma curvieri* (Weitere Untersuchungen der Gonaden von *Rhizostoma Cuvieri*). Haurowitz (F.), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1922, 122, 145-159.

A tabulation of the various chemical compounds isolated from or identified in the gonads of the organism mentioned in the title.

—F. S. H.

(GONADS) Solid sarcoma of the OVARY. Hoon (M. R.), Penn. M. J. (Harrisburg), 1922, 26, 30-32.

A general review of the literature on this subject. The author arrives at the following conclusions: approximately 20% of all ovarian tumors are malignant; solid sarcoma of the ovary is the rarest type of ovarian tumor (1% is the approximate incidence); the tumor most commonly occurs in those under three years, and is decreasingly common up to 14 or 15 years; the two periods of usual occurrence in adults are during the third decade and after the menopause; and the prognosis in adults is better than in children.—I. B

(GONADS) The action of PLACENTA extract on salivary secretion (Ueber die Wirkung von Placentaextrakten auf die Speichelsekretion). Kosakae (J.), Biochem. Ztschr. (Berl.), 1922, 130, 249-251.

Placenta extract stimulates secretion from the salivary glands of dogs. Two animals were used. The heating of the extract to

130° destroys the stimulating effect. The action is not increased by simultaneous administration of pituglandol.—F. S. H.

(GONADS) Degeneration of conserved OVARIES after hysterectomy in rat; an experimental study. Kross (I.), *Am. J. Obst. & Gynec.* (St. Louis), 1922, 4, 408-412 (Oct.).

As a result of experimental work upon young but sexually mature rats, Kross concludes that conservation of sound ovaries when the uterus is removed is of no avail in preventing menopause symptoms. The dangers of cystic and other degenerative changes are so great that the retention of the ovaries constitutes a serious danger, and it is safer to remove the ovaries in all cases where hysterectomy is performed.—E. N.

(GONADS) Hypogenitalism from the experimental viewpoint (L'ipogenitalismo dal punto di vista sperimentale). Lipschütz (A.), *Rassegna di studi sessuali* (Roma), 1922, 2, 132-146.

In cases of hypogenitalism the sexual gland may be involved first, or the syndrome may be caused primarily by some other endocrine disturbance; in either case, however, the endocrine sexual gland is always involved. In woman there is a parallelism between the quantitative variations of the endocrine functions in the ovary and sexual manifestations. This is not true in man; there is either normal function with even a minimal residue of testis or no function at all. The few cases of eunuchoidism obtained with conservation of testicular tissue are due either to delayed or hindered development, due to the operation being performed before the testis reaches maturity. There are cases of eunuchoidism in which such a cause cannot be found, however. As an explanation of such cases the author claims that the psychosexual reaction does not depend alone on the sexual gland, but also upon the functional condition of the transformers and of the nervous paths; therefore he does not consider it rational to treat quantitative sexual insufficiency with sexual or other hormones.—G. V.

(GONADS) Eunuchoidism in rabbits due to underdevelopment of the TESTES (Über Eunuchoidismus beim Kaninchen, bedingt durch Unterentwicklung des Hodens). Lipschütz (A.), Ottow (B.) & Wagner (K.), *Arch. f. Entwicklungsmechn. d. Organ.* (Berl.), 1922, 51, 66-78.

Three rabbits from the same litter when one month old were partly castrated, and the ductus epididymidis cut. Only from $\frac{1}{4}$ to $\frac{1}{2}$ of the testicular tissue was left. When killed $2\frac{1}{2}$ to 7 months after the operation they had the appearance of fully castrated animals. The tubules in the remaining portions of the testis at the time of death were either infantile or abnormal in appearance. The interstitial cells were also infantile. In one case the Sertoli cells

were very numerous and yet the castration effects had not been prevented; hence these cells alone are not the internal secreting elements of the testis. Young germinal cells were present and therefore are not to be regarded as the internal secreting structures. This leaves as the probable source of the internal secretion either the interstitial cells or those stages of the germinal cell cycle which were absent.

—A. T. R.

(GONADS) OVARY and sexual desires (*Eierstock und Geschlechts-trieb*). Mansfield, *Klin. Wchnschr.* (Berl.), 1922, 1, 1760.

The author often observed that women in whom there had been autoplasmic transplantation of little pieces of ovary (method of Unterberger) became very erotic.—J. K.

(GONADS) Genitodystrophia and HYPOPHYSEAL geroderma from hereditary syphilis (*Geroderma genitodistrofico ed ipofisario da sifilide ereditaria*). Mariotti (E.), *Gior. malattie nenerree*, 1921, No. 2; abst., *Pathologica* (Geneva), 1922, 14, 346 (June).

There is a variety of the gerodermic type in which, besides genital dystrophy, there is hypophyseal dystrophy, with probable involvement of the thyroid and adrenal glands. This dystrophic anomaly may be due to hereditary syphilis and constitutes a morbid type of its own,—a morphologic variety in hereditary lues. Early diagnosis and specific treatment, before puberty or when puberty is due, can partially modify the morphology and stimulate a virility which otherwise would never have been manifested.—G. V.

(GONADS) OVARIAN transplantation. Martin (F. H.), *Surg. Gynec. & Obst.* (Chicago), 1922, 35, 573-585 (Nov.).

The sixth of a series of studies of this subject which the author has published from time to time (1903, 1908, 1911, 1915, 1917, 1922). He summarizes his impression of the whole subject by saying that, as more evidence is accumulated from the literature, the claims of the earlier enthusiasts seem to become less and less substantial. His conclusions are as follows. Clinically, there is very little to encourage one to believe that transplantation of the ovaries, as practiced up to the present time, has more than speculative value as a surgical procedure. There is some evidence that autotransplants are of some value in deferring the symptoms of the menopause and delaying the cessation of menstruation. It is difficult, however, not to attribute some of this evidence to suggestive therapeutics or to unattached ovarian tissue left in situ. There is practically no convincing evidence that homotransplants and none that heterotransplants have been successful in the human female. There is some encouraging evidence recorded in experimental animal surgery that not only autotransplants, but homotransplants and even heterotransplants have been successful and the sexual function of

the castrated animal maintained. The technique followed by the various operators on women in too many instances seems unsurgical, and too often is incompletely and loosely recorded, leaving the impression that the conclusions must be unreliable. There is, however, encouraging evidence in all of this endeavor to lead one to hope that the subject will be pursued experimentally, especially for the purpose of devising a rational and simple technique, based on the work of the serologists, the endocrinologists, the hematologists, and the practical clinical surgeons. A complete bibliography, embracing 147 references, accompanies the article.—E. N.

(GONADS) Some aspects of the problem of sterility. Meaker (S. R.), Boston M. & S. J., 1922, **187**, 535-539.

Preparations of the whole ovary and thyroid are useful in combatting symptoms in some types of sterility, but ineffective in treatment of the condition itself. The author refers to the endocrine aspects of the problem only very briefly.—J. C. D.

(GONADS) Lateral partial hermaphroditism. Moots (C. W.), Am. J. Obst. & Gynec. (St. Louis), 1921, **1**, 864-867 (May).

A case report of a patient of 27 years who had had amenorrhea and hypertrichosis of the male type since the age of 21. The external genitalia were normal except that the clitoris was much enlarged, being 1 inch long. A solid mass was felt at the left of the uterus. Organotherapy failing, laparotomy was performed. The author states that the mass proved to be a "fibroblastic sarcoma of the embryonic testis." On the 28th day after operation, the menses started, and the flow continued throughout the year. The hair became much finer and softer as well as much slower in growth. The patient died of influenzal pneumonia 23 months after the operation.—E. N.

(GONADS) The function of CORPUS LUTEUM (La función de los cuerpas amarillos). Quinterno (A. F.) These of Buenos Aires (Argentine), 1921, No. 3999.

Uninfluenced by previous observations, the author investigated the action on guinea pigs and rabbits of soluble substances in acetone and chloroform from corpus luteum of cows. The corpus luteum was desiccated at 45° C., triturated, extracted with acetone by Soxhlet apparatus, evaporated and dissolved by chloroform. This substance was taken by oil or saline solution and injected intravenously or intraperitoneally in doses of 0.03-0.05 cgrs. The author concludes that this substance does not affect the gonads, is a vasodilatador, and influences the adrenals.—G. P. G.

(GONADS) Un caso de INFANTILISMO. Rodríguez Molina (L. F.), Rev. méd. cubana (Habana), 1920, **31**, 654-656.

(GONADS) Cells of internal secretion in the OVARY and osteomalacia (*Cellule a secrezione interna dell' ovaio ed osteomalacia*). Spirito (F.), Congr. soc. ital. di ostet. e ginec., 1921 (October); abst., Rassegna internaz. di clin. e terap. (Napoli), 1922, 3, 45 (January).

From the histological examination of ovaries taken from cases of gravidic as well as non-gravidic osteomalacia and of ovaries removed for other causes in different periods of sexual activity the author concludes that no important significance can be ascribed to their lipid content.—G. V.

(GONADS) Treatment of OVARIAN hemorrhages (*Behandlung ovarieller Blutungen*). Stickel, Klin. Wehnschr. (Berl.), 1922, 1, 1760.

Nearly all extracts of endocrine organs contain a hemostatic substance. The best is an extract from testicles and pituitary with calcium. This preparation is called coluitrin calcium and must be given intravenously.—J. K.

(GONADS) Four cases of false pregnancy (*Cuatro casos de falso embarazo*). Torre Blanco, An. Acad. méd. quirurg. españ. (Madrid), 1921, 9, 448-452.

Pseudocyesis is attributed to ovarian insufficiency.—E. B.

(GONADS) On the interstitial cells and spermatogenic tissue in a case of eunuchoidism in the rabbit (*Über die Zwischenzellen und das spermatogene Gewebe in einem Fall von Eunuchoidismus beim Kaninchen*). Wagner (K.), Arch. f. Entwicklungsmechn. d. Organ. (Berl.), 1922, 51, 416-435.

Two out of three rabbits from the same litter were unilaterally castrated when 1½ months old. Five months later, while spermatogenesis seemed to be about equally active in all three animals, the volume of the testicular tubules in the remaining testis of the partly castrated animals was about double that of one testis of the control animal. But since the control had two testes, the total amount of testicular substance was about the same in all three cases. There was about the same number of interstitial cells, but their size varied. One of the castrated animals had interstitial cells which were larger than in the normal, largely due to coarse granules in the cytoplasm. This animal had a penis which was practically normal in size. In the other castrated animal, the interstitial cells were distinctly smaller than normal, and the penis in this case was underdeveloped. The conclusions drawn are that the interstitial cells are necessary for the post-pubertal development of the external male genitals, that a sexual hormone is produced by the interstitial cells, and that spermatogenesis can go on in spite of underdeveloped interstitial cells. Only a few specific references are given.—A. T. R.

(GONADS) Methodical therapy in the vomiting of pregnancy (Thérapeutique methodique des vomissements gravidiques). Wallich, Gynéc. (Par.), 1922, 21, 486.

Chloral hydrate plus corpus luteum or adrenal is advocated. No details.—F. S. H.

(GONADS) The interstitial gland. Williams (L.), Brit. M. J. (Lond.), 1922, i, 833-835.

A general article in which the author theorizes, among other things, to the effect that the interstitial cells play a part in the determination of sex.—W. J. A.

Development of GONADS and transformation of sex in the frog. Witschi (E.), Am. Naturalist (N. Y.), 1921, 55, 529-538.

It is stated that the gonads of certain frogs contain both egg and sperm producing cells, which develop at different times. "Under natural conditions most individuals develop first ovaries, which later on are transformed into testes. During this transformation the gonads, showing the characteristics of both sexes, are hermaphroditic; but without exception the female characters become reduced and mostly disappear completely."—W. J. A.

Arterial hypertension due to insufficiency of the GONADS (Hypertension artérielle par insuffisance des glandes génitales). Zénope (P.), Rev. franç. de gynéc. et d'obst. (Par.), 1922, 17, 401-405 (July).

In a systematic study of the arterial tension in about a hundred patients from the standpoint of the endocrine glands the author was struck by an apparent relation between the blood pressure and the ovaries or testes. In men, the tension varies inversely with sexual potency, and in women, with the quantity of menstrual flow. Whenever the periods commence to diminish, as at the menopause, the blood pressure, it is stated, begins to rise. The author favors the view that the hypertension is the result of the hypogonadism, and explains the occurrence as due to hyperthyroidism produced by hypogonadism.—E. N.

The cell division hormones and their relations to wound healing, fertilization, parthogenesis and to adventitious embryonism (Ueber Zellteilungshormone und ihre Beziehungen zur Wundheilung, Befruchtung, Parthogenesis und Adventivembryonie). Haberland (G.), Biol. Zentralbl. (Berl.), 1922, 42, 145-171.

Isolated plant cells divide only if brought into contact directly or indirectly with fragments of leading bundles (Leptoma). Even cell divisions which effect the formation of "wound-cork" (Wundkork) appear only under the influence of a "cell division hormone,"

a stimulating substance, originating from the vessel bundle. (Experiments with potato sprouts, stalks of *Sedum spectabile*, etc., leaves of crassulaceas, etc.). Certain substances, appearing at dissolution of mechanically damaged cells, work as "wound hormones," inciting cell division. Single injured cells surrounded by intact tissue undergo division under the influence of "wound hormones" produced by themselves (experiments with stalk and leaf-hairs of *Coleus hybridus*, *Pelargonium zonale*, etc.). Traumatic parthogenesis depends upon the origin of "wound hormones" within the injured egg cell. (Bruise of castrated flower buds of *Oenothera lamarckiana* causes disposition to parthogenetic development of the egg cell). The fruit-bud being damaged by punctures can originate more or less typical adventitious-embryones, proceeding from the nucellus or from the seed germ. Therefore, it seems probable that even the natural, habitual adventitious embryonism depends upon "necro-hormones," produced by the dissolution of nucellar tissue cells. Even the natural parthogenesis in some plants (especially *Taraxacum officinale*) is evidently the consequence of the perishing of integument cells and necro-hormone production. In several composita "wound endospermata" and "endospermic embryones" have been observed after natural necrotic processes within the embryo sack. The initiation of development in such egg cells, which need fertilization, seems to be due to (a) injury of the egg cell by the entering spermatozoon; (b) substances, produced by dissolution of the spermatozoa. In cases of "pseudogamism" several spermatozoa enter into the egg cell, but none of them unites with the nucleus. The cells' development is evidently caused by the irritation occasioned through their entering and by the products of their dissolution. In the farther development the embryonic tissue itself seems to furnish the necessary hormones. In higher developed plants we can therefore distinguish hormones from the embryo and the meristem, hormones from the leptoma, and wound- and necro-hormones.—A. B.

Influence of HYPOPHYSEAL extracts and of lesions of the nasal pharynx on the cellular metabolism of the HYPOPHYSIS (*Influenza di estratti ipofisari e di lesioni del faringe nasale sul metabolismo cellulare dell' ipofisi*). Basile (G.), Riv. de patol. nerv. (Firenze), 1919, 24, 257-282 (December).

The present study is based on the possible correlation between pharyngeal lesions and the hypophysis as deduced by Citelli, who (accepting the existence of a normally functioning "pharyngeal hypophysis" in extra-uterine life, similar to the anterior lobe of the cerebral hypophysis) believes that diseases of the pharyngeal roof as well as of sphenoidal sinuses have a possible influence on hypophyseal pathology and that there is a possible hypophyseal pathogenesis of some symptoms or groups of symptoms that are apt

to occur in such diseases. Previous experiments on both rabbits and dogs (i. e., in animals with open and closed pharyngeal canal) showed that lesions of the roof of the pharynx determined inflammatory reaction in the cerebral hypophysis and that hypophyseal medication in such cases proved of some value, just as it did with patients with pharyngeal and hypophyseal symptoms. The author reports his recent experiments of lesions of the roof of the pharynx of rabbits and dogs followed by hypophyseal medication, in which the following results were obtained. Cauterization of the roof caused decided hypophyseal reaction (eosinophils, granules and lipid vesicles) which became even more evident if followed by injections of hypophysis extract. The injections alone induced hyperplasia of the elements of the hypophysis, in proportion to the number of the injections. Cauterization of the hard palate had no effect on the hypophysis. The author insists that the hypersecretion following the cauterization is abnormal, while the hyperplasia and hypersecretion following hypophysis medication is normal, because the latter leads to a return of the normal function of the gland, as is demonstrated in animals killed after the inflammatory reaction induced by the cauterization had subsided.—G. V.

(GONADS) **Hiperchloridria por HIPOOVERISMO.** Bermijillo (M.), *Siglo méd. (Madrid)*, 1922, 69, 655-656.

Opinions vary as to the relations between the ovary and hyperchlorhydria; nevertheless, the author postulates the existence of hyperchlorhydria in menstruation, pregnancy and chlorosis. Bermijillo refers to a case of intense hyperchlorhydria in a young woman with ovarian insufficiency that he cured by opotherapy after having been unsuccessful with medicines in current use.—E. B.

(HYPOPHYSIS-THYROID) Pituglandol to combat dwarfism (Pituglandol gegen Zwergwuchs). Bleuler (E.), *Schweiz. med. Wchnschr. (Basel)*, 1922, 52, 703.

A 12 year old boy who for at least a year had ceased to grow and was losing weight for no evident physical reason, resumed normal growth when given pituglandol in connection with thyroidin, though neither of these alone gave results. Daily doses of 3 to 4 grains of pituglandol solution may temporarily produce loose and tender teeth.—A. T. R.

(HYPOPHYSIS) Cranial trauma, DIABETES INSIPIDUS, trephination (Trauma cranico: diabete insipido—trapanazione). Catterina (A.), *Policlin. (Roma)*, 1920, 181; abst., *Pathologica (Genova)*, 1922, 14, 183.

Report of a case of a man 40 years old who had a severe injury of the cranium with probable fracture of the base. The trauma was followed by diabetes insipidus, which was probably due to pressure

on the infundibulum or on the tuber cinereum. Trephination was performed in the left frontal region and the diabetes insipidus disappeared.—G. V.

HYPOPHYSIS in brain lesions (*Iposisi nelle lesioni del cervello*).

Desogus (V.), Soc. sc. med. (Cagliari), 1921; abst., *Pathologica* (Genova), 1922, 14, 337-338 (June).

The author started his experiments on hypophysis of dogs in which either the occipital, the parietal or the frontal lobe had been destroyed in both hemispheres. He chose about 50 animals of the same size, weight and age (one to two years old); he used only those in which healing was by first intention, and which, before being sacrificed, had wholly recovered to the point of often being taken for normal. The point of the brain cortex destroyed did not alter the results. In the animals sacrificed from 20 to 30 days after the trauma, there was found hypophyseal hyperfunction with intense hyperemia, intense eosinophilia and secretion of colloid; also eosinophil substance (only basophil in the paranervous lobe) was detectable within the parenchyma near the cells, which secreted it. In the animals killed from the 30th to the 60th day the eosinophils began to turn pale and their nucleus became pyknotic, while the fundamental cells became quite evident. The sinusoidal capillaries, which in the above series appeared hyperemic, appeared full of colloid, which, treated with eosin-hematoxylin, looked from dark yellow to brick red. On superficial examination it reminded one of the thyroid. The glandular parenchyma was lacunar as if disintegrated on account of the previously secreted colloid, which by being absorbed by the capillaries left empty the spaces which were previously occupied. Analogous phenomena were observed in the nervous lobe (which was studied from its secretion startpoint). The nuclei of its cells became small and pyknotic, its capillaries and blood sinuses showed colloid with the same characteristics as that in the anterior lobe. The paranervous lobe, which kept its basophilic characteristic, showed the same amount of dissociation between its elements as the anterior lobe, and its hyaline substances was very copious in the alveoli proper. In the animals killed from the 60th to the 90th day after the trauma, the eosinophils were pale and their nuclei totally pyknotic. The nuclei of the basophils underwent analogous transformation, while the fundamental cells were still numerous and did not show any condition of pyknosis. The colloid became colorless, almost "mother of pearl," but it was in such a great amount as to break the walls of the capillaries in places and to invade the parenchyma, isolating and drowning the cells to a great extent and forming real colloidal lakes. In the nervous lobe an enormous amount of colloid invaded the stroma; the nuclei were either small, or irregular, or very large or pyknotic. As soon as the colloid had been reabsorbed, the hypophysis appeared to be in a

condition of absolute rest; there was evident basophilia and the hyaline substance of the paranervous lobe looked lacunar and dissociated. In the animals killed after the 100th day there was functional reintegration of the hypophysis; the nuclei appeared normal, the circulation was active and gradually the eosinophilia was re-established. Desogus quotes analogous results obtained by Ceni, who used the same experimental method, in the thyroid and adrenals, and opposite results obtained by the same author in male and female gonads. Ceni consequently stands for the existence of special visceral centers scattered upon the cerebral cortex, which regulate the sexual glandular functions—superior genetic centers—and for the existence of endocrine glandular centers controlling the corresponding functions. He calls the former “genetic” and attributes to them an exciting function controlling the sexual glands, male and female.—G. V.

Studies on the PITUITARY. I. The melanophore stimulant in posterior lobe extracts. Hogben (T. L.) & Winton (E. R.), *Biochem J.* (Cambridge, Eng.), 1922, 16, 619-630.

The pars intermedia of the mammalian pituitary secretes a specific stimulant inducing expansion of the dermal melanophores of amphibia. This property is shared by extracts from birds, reptiles, amphibia and fishes. It was not found in the sub-neural gland of Tunicates. The reaction is extremely delicate and apparently specific except as regards large doses of nicotine or apocodeine. The activating agent is destroyed by tryptic, but not by peptic digestion. The probable identity of the uterine stimulant with the melanophore stimulant is established. The use of the reaction in testing pituitary extracts is advocated.—F. S. H.

(HYPOPHYSIS) Effect of injection of extract of anterior lobe of pituitary gland upon the organs of generation. Kross (I.), *Am. J. Obst. & Gynec.* (St. Louis), 1922, 4, 19-26 (July).

Since feeding the extract is attended by the possibility that the animal might not consume and retain the entire dose, and that digestive changes might render it inert, the substance was given hypodermically. Fifty-two white rats were injected subcutaneously every day except Sundays with antuitrin (a water-soluble preparation of the anterior lobe of the hypophysis, prepared by Parke Davis & Co.) in doses of 0.2 cc., equivalent to 0.005 gm. of the desiccated powder. With few exceptions the pituitary-fed animals weighed less than the controls. In all cases the ovaries of the pituitary-fed animals showed the same or less activity than the controls, possibly as a result of the frequent injections of foreign proteins. In none of the sections could any evidence be found of an earlier sex maturity in the pituitary-fed animals.—E. N.

The **HYPOPHYSIS** and **canalis craniopharyngeus** in nine cases of **cranioschisis** (*Das Verhalten der Hypophyse und des Canalis craniopharyngeus in neun Fällen von Kranioschisis untersucht*). Mauksch (H.), *Anat. Anz. (Jena)*, 1921, 51, 248-264.

Gross and histological examination of the hypophysis and related structures in 9 cases of congenital cranial defect with **anencephalia** (267 to 500 mm. standing height) showed that while there was a hypophysis present in every case, in only 2 were all three lobes present. The posterior lobe, which was present in only 2 cases, was underdeveloped and otherwise abnormal. In these two cases there was no brain tissue. The intermediate lobe was deficient simultaneously with posterior lobe deficiency, as if *pars intermedia* depended upon the presence of *pars posterior*. The presence of an anterior lobe was entirely independent of the existence of the other lobes. The general shape of the hypophysis (measurements of diameters are given) was generally abnormal. The *sella turcica* was frequently greatly flattened out. The **canalis craniopharyngeus** varied greatly from the normal, being complete in 5 cases and incomplete in 4 cases. The contents (connective tissue, blood vessels and epithelial elements) of the canal are described. Five references are given.—A. T. R.

(**HYPOPHYSIS**) Pituitary extract and **metrorrhagia** (*Extrait hypophysaire et métrorragies*). Mossé (S.) & Fabre (M.), *Gynéc. et Obst. (Par.)*, 1922, 5, 228-230 (Mar.).

The therapeutic effect of pituitary extract depends on its constricting action upon the uterine musculature, its vaso-constrictor effect on the utero-ovarian vessels, and its action in lessening the internal secretion of the ovary. It is especially indicated in the **metrorrhagias** of puberty, which are the consequence of hyper-ovarium, and those of the menopause, which are due to ovarian excitation. In emotional **metrorrhagia**, in which there is ovarian hypersecretion of emotional origin, hypophysis extract has given good results. In **metrorrhagia** of fibroids, surgical treatment or radiotherapy is preferable, and the results in hemorrhagic metritis are mediocre. Since pituitary extract tends to cause hypertension, the heart, blood pressure and urine should be examined during the treatment.—E. N.

INFANTILISM of **HYPOPHYSEAL** type and the **Argyll-Robertson** sign, together with a tumor developed at the tip of the thalamic portion of the third ventricle infiltrating the optic tract, but not invading the region of the infundibulum or **HYPOPHYSIS** (*Infantilisme du type hypophysaire et signe d' Argyll-Robertson, avec tumeur développée au niveau de la partie thalamique du troisième ventricule et infiltrant les couches optiques, mais envahissant pas la région de l'infundibulum ni l'hypophyse*). Ricaldoni (A.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, 46, 1238-1249.

Diabetes insipidus accompanied the condition described in the title.—F. S. H.

(HYPOPHYSIS) Effective constituents of the **PITUITARY** body. II. Communication. Saito (Y.), Tokyo Igakkai Zasshi, 1922, 36, No. 5 (May).

The author proved that the efficacious constituents consist of two substances; one is histamine and the other is a substance that contracts the uterus and augments the blood pressure. The latter substance is decomposed by being boiled in alkaline solution, and thus it bears a close resemblance in these respects to adrenalin.

—Jap. Med. World, 2, 302.

HYPOPHYSEAL obesity syndrome with glycosuria following a wound of the frontal lobe (*Syndrome d'obésité hypophysaire avec glycosurie consécutive à une blessure du lobe frontal*). de Teyssieu (M.), Rev. neurol. (Par.), 1922, 20, 1020-1021.

The patient had a wound of the left frontal lobe producing comparatively little injury with apparent recovery after operation. He developed headaches and periodic generalized convulsions. The weight after injury was 58 kg.; six years later it was 95 kg. The appetite was increased; the sexual power was diminished. The urine showed 100-150 gm. of sugar in 24 hours. Muscular power was diminished. He had no beard and the body was smooth. Mentally he was sluggish, irritable and emotionally unstable. No x-ray abnormalities in the region of the sella turcica were seen. The Wassermann test and cerebrospinal fluid were negative.—C. E. N.

(HYPOPHYSIS) Parkinson's disease and dystrophia adiposogenitalis associated with postmeningoencephalomyelitis (*Syndrome Parkinsonien et syndrome adipo-génital associés postméningoencéphalomyélique*). Potet (M.), Rev. neurol. (Par.), 1922, 20, 1024-1028.

Report of a patient, aged 27 years, with the Parkinsonian type of encephalitis and presenting also the Froehlich-Babinski-Launois adipo-genital syndrome (obesity, non-painful polysarcia, hypotrichosis, impotency and puerilism).—C. E. N.

(HYPOPHYSIS) Dyspituitarism, obesity and infantilism. Tidy (H. L.), Lancet (Lond.), 1922, ii, 597-602.

Tidy reviews in a general way our present knowledge of the pituitary body, as regards anatomy, development, physiology and clinical manifestations of pituitary disorders. Over-secretion of the anterior lobe before union of the epiphyses produces gigantism; after union, acromegaly. Under-secretion before puberty causes Lorain type of infantilism; after puberty, a condition which is unrecognized. Over-secretion of the posterior lobe brings about an

unrecognized condition; under-secretion causes diabetes insipidus. Diminution of secretion of the whole gland produces dystrophia adiposogenitalis, syndromes of adiposity, genital dystrophy and infantilism, varying in type according to whether it commences before, during, or after puberty. Treatment of these various conditions is conservatively discussed as being largely in the experimental stage. The parenteral use of posterior lobe extract in diabetes insipidus and the use of pituitrin in obstetrics, in meteorism and in shock are pointed out as well established therapeutic procedures.

—I. M.

(HYPOPHYSIS) A case of cured **DIABETES INSIPIDUS** (Geheilte Fall von Diabetes insipidus). Umber, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1221.

The patient, a man of 41, had bitemporal hemianopsia. He had very painful headaches and became blind. The sella was normal. The Wassermann reaction in the blood was positive; in the cerebrospinal fluid, negative. Antisymphilitic treatment was followed by complete recovery.—J. K.

The action of the extract of the posterior lobe of the **HYPOPHYSIS** (Sul' azione dell' estratto di lobo posteriore di ipofisi). Villa (L.), Arch. di patol. e clin. med. (Bologna), 1922, 1, 152-164 (January).

Villa investigated whether the gastric reaction to post-pituitary extract was due to a peculiar action on the general water balance. He noted a very definite action of the extract on the salivary as well as on sudoriferous secretion. From these data and a study of the literature on gastro-enteric secretion, urinary and milk secretion, the author concludes that the extract does affect the water balance, but thinks that this conclusion is not precise enough as applied to phenomena so complex and with activities of such different character. Therefore, he takes into consideration not only the action of the extract, but the various peculiarities of action of the several excretory and secretory systems. He agrees with Houssay that it is impossible to deduce the physiological properties of the hypophysis from the action of the extract.—G. V.

Erythropoietic center in the HYPOPHYSIS of the pregnant guinea pig (Foyers d'erythropoiese dans l'hypophyse de cobaye gravide). Watrin (J.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 1038-1039.

Histological.—T. C. B.

HYPOPHYSEAL lesion in a case of progressive lipodystrophy (Reperto anatomo-patologico di lesione ipofisaria in un caso di lipodistrofia progressiva). Zalla (M.), Riv. di patol. nerv. (Firenze), 1920, 25, 25-37 (April).

Report of the post-mortem examination of a case of progressive lipodystrophy in a woman 59 years old. The chief lesion, besides a complete fibrosis of the ovaries, was a quantitative change in the anterior pituitary. The elements still found showed signs of intense functional activity.—G. V.

The biological action of LYMPH-GLAND extracts on smooth muscle tissue, the heart and the blood-pressure (Ueber die biologische Wirkung von Lymphdrüsenextrakt auf Organe glatter Muskulatur, auf das Herz und den Blutdruck). Wirth (O.), *Biochem. Ztschr.* (Berl.), 1922, **132**, 245-269.

Water and alcohol extracts of lymph glands from different animals and different portions of the body were tested in vivo and in vitro. All aqueous extracts, whether obtained by cold or hot extraction or from fresh or heated tissue, had the same qualitative effect on surviving tissues containing smooth muscle. The isolated blood vessels reacted the same as towards adrenin—by contraction, save the coronary artery of the bovine species which relaxed. The vessels of the hind legs of the frog were dilated by both weak and concentrated solutions. The intestine and virgin and gravid uterus responded with an increase in tone. The alcohol extracts differed both quantitatively and qualitatively from the aqueous extracts. The isolated blood vessel strips contracted. The vessels of the hind legs of the frog dilated after weak doses, dilated and then contracted or vice versa after medium doses and contracted after concentrated doses. This latter contraction was followed by a dilatation. The tonus of the intestine and uterus was raised. An analysis of the qualitative reaction of the two extracts on the coronary artery demonstrated the presence of two antagonistic principles. The extraction of the aqueous extract with ether caused separation of the hypotonic from the hypertonic element, as present in the alcohol extract. The effect of the aqueous and alcohol extract on the curarized frog heart in situ was studied in detail. Two phases occurred. In the first there was decrease in the amplitude of contraction and slight decrease in tonus. In the second phase the frequency decreased while the amplitude increased. Hearts that are beating badly can be stimulated to stronger function by the application of lymph-gland extract. There is no general antagonism between adrenalin and this extract. The action of the alcohol extract simulates that of cholin. The blood pressure is lowered on exhibition of the extracts.—F. S. H.

I. Effect of PANCREATECTOMY and ADRENALECTOMY on heat production in the frog. II. THYROID physiology in the frog (I. La produzione di calore nella rana apancrata e nella rana privata delle capsule surrenali. II. Contributo allo studio della fisiologia della tyroide della rana). Gayda (T.), *Gior. d. r. Accad. di med. di Torino*, 1922, **84**, 401-407; *Arch. de sc. biol.*, 1922, **3**, 415-423.

I. Removal of the pancreas has no influence on heat production in frogs. After partial removal of the adrenals the production of heat decreases to 30%. If, in consequence of the operation, the remains of the adrenals become necrotic, a further diminution is observed on the day preceding the death of the animals. II. The removal of the thyroid, the feeding on thyroid, and the grafting of pieces of the same gland have almost no effect on heat production in adult frogs.—Physiol. Abst., 7, 371.

The PINEAL gland (Lo stato attuale delle nostre conoscenze sulla ghiandola pineale). Orlandi (N.), Osp. maggiore (Milano), 1922, 10, 223-233 (August).

A thorough review of the pineal literature.—G. V.

Pathology and symptomatology of TETANY III (Beiträge zur Pathologie und Klinik der Tetanie III). Elias (H.) & Kornfeld (F.), Arch. f. innere Med., 1922, 4, 191-208.

A study carried out on 7 patients. The blood in tetany absorbs the same quantity of CO_2 as normal blood. Ingestion of even large quantities of HCl had no influence on the clinical picture. Some American authors have stated that ingestion of alkali affects the disease. Elias and Kornfeld never could confirm this; on the contrary, good results were often obtained when sodium carbonate was injected intravenously during the attacks. The same effect was also seen, however, from intravenous injections of neutral hypertonic solutions. An unfavorable result was seen after the ingestion of H_2PO_4 , due probably to the HPO_4 ion which seems to have an especially bad influence on tetany.—J. K.

Calcium deficiencies. Their treatment by PARATHYROID. Grove (W. R.) & Vines (H. W. C.), Brit. M. J. (Lond.), 1922, i, 3203 (May 20).

After quoting evidence from previous papers regarding the presence of ionized and combined calcium in the circulating blood and concerning the fact that when the parathyroid glands were injured tissue resistance was decreased, these authors report a long series of cases of chronic toxemias and conditions of uncertain origin in which parathyroid was given with good results. They first estimated the blood serum calcium (combined and ionic) and then gave the parathyroid gland until the normal percentage was restored. They conclude that by parathyroid therapy it is possible to rectify the calcium balance of the blood serum more effectively than by the injection of calcium salts. The therapeutic action of parathyroid substance is physiological, i. e., its action is to place the tissues of the patient under conditions more suitable for the performance of their normal function and for combatting the effects of toxic processes.—F. C. P.

The diffusible calcium of the blood serum. II. Human rickets and experimental dog TETANY. von Meysenburg (L.) & McCann (G. F.), *J. Biol. Chem. (Balt.)*, 1921, **47**, 541-546.

Studies on parathyroidectomized dogs as compared with cases of human rickets showed that the diffusible calcium of the serum in both types of disorder is between 60 and 70 per cent of the total serum calcium, a range within the normal. Hence tetany probably is not due to a lowering of the diffusible as contrasted with the non-diffusible form.—F. S. H.

Enlarged THYMUS. Barbour (O.) & Goin (L. S.), *Illinois M. J (Oak Park)*, 1922, **42**, 299-304.

A general review. Six case reports are included. The authors conclude that thymic hyperplasia is probably more common than is usually recognized. Diagnosis of this condition can be established by the proper combination of clinical and x-ray findings. The majority of these cases are cured or greatly improved by the proper application of radiant energy. Radium seems to have some advantages over the x-ray in the treatment of such conditions.—I. B.

The function of the THYMUS (*Concepto actual de la function del timo*). Bonilla, *Méd. iberica (Madrid)*, 1922, **16**, 181-184.

Bonilla gives a résumé and a detailed criticism of the contradictory reports which have recently appeared as to the function of the thymus. He concludes that no one knows just what the function of this organ is; however, he differs with those authors who deny that the thymus is an endocrine gland.—G. M.

Treatment of psoriasis with extract of THYMUS (*Behandlung der Psoriasis vulgaris mit Thymusextrakt*). Gross (B. G.), *Deutsche med. Wchnschr. (Berl.)*, 1922, **48**, 1211.

In some very severe cases of psoriasis excellent results were seen from intramuscular injections of extract of thymus. Generally 8-14 injections of 1 cc. (equivalent to 5 gm. gland substance) were enough to cure the disease.—J. K.

Structural modifications of the THYMUS in partially thymectomized chickens (*Modificazioni strutturali del timo in polli incompletamente stimizzati*). Pighini (G.), *Biochem. e terap. sper. (Milan)*, 1922, **9**, 37-40 (February); abstr., *Pathologica (Genova)*, 1922, **14**, 319-328.

The author reports the case of two chickens in which cachexia after thymectomy appeared later than in controls. None of the cortical or lymphocytic elements was left in the remaining thymus, but there was an enormous development of somewhat abnormal Hassall's corpuscles.—G. V.

Respiratory exchange and basal metabolism in **THYROID** syndromes (Les échanges respiratoires et le métabolisme basal dans les syndromes thyroïdiens). Achard (C.) & Binet (L.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1217-1222.

The influence of the **THYROID** on restoration of fractures (Influenza della tiroide sul decorso di guarigione delle fratture). Agresti (E.), Rassegna internaz. di clin. e terap. (Napoli), 1922, 3, 286-297 (July).

Agresti induced fractures in young and adult rabbits at different periods after thyroidectomy. When fractures were induced in adult rabbits a few days after thyroidectomy, although the evolution of the fracture did not differ from that of the controls, the involution of the callous was hastened, the callous resembling a porous bone 90 days after the fracture. Young rabbits showed no difference from the controls in the evolution of the fracture; the involution of the callous could not be studied, owing to intervening cachexia and deficiency of material. The fractures induced in rabbits 60 days after thyroidectomy showed a very slow and incomplete recovery, for while the periosteum reacted normally there was constant necrosis of the ends of the fractured bones. The same result was obtained in young cachectic rabbits, and when the condition was very low even the periosteum showed less activity.—G. V.

Influence of the **THYROID** on the leukocyte formula in Graves' disease (Ricerche sperimentali riguardanti l'influenza della tiroide sulla formula leucocitaria del sangue a proposito della linfocitosi dei Basedowiani). Baggio (C.), Arch. per le sc. med. (Torino), 1920, 43, 93-127; abst., Pathologica (Genova), 1922, 14, 146 (March).

While thymectomy experiments showed by diminution of leukocytes that the thymus has an influence on the leukocyte formula of the blood, thyroidectomy experiments did not show this. Since leukocytosis is not peculiar to Graves' disease, but also occurs in myxedema—spontaneous as well as following operation—these results suggest that leukocytosis in Graves' disease is not due merely to thyroid hyperfunction. For the same reason it should not be ascribed to the thymus as in some way influenced by the special secretion of the Basedowian thyroid. This condition of leukocytosis may be a general manifestation of the organism, vagotonically altered on account of an initial cause, which, in exophthalmic as well as in other goiters, may be acquired and is more or less influenced by congenital dispositions. In cases of homologous athyreosis it is no doubt congenital. The author concludes that the Basedowian thymus no doubt is a contributing factor in leukocytosis as it is an endocrine organ of the vagus, to which and from which stimuli go.

—G. V.

(**THYROID**) **HIPERTIROIDISMO e infecciones locales.** Bonilla, Méd. iberica (Madrid), 1921, No. 211, 413-415.

A critical exposition of the modern theories which attribute great importance to small focal infections in the genesis of hyperthyroidism. The author recognizes the value of this hypothesis, but does not favor exaggerations of its importance. He believes it to be inadvisable to extirpate the tonsils (whose functional importance we do not know) or to take out all the teeth which are slightly infected, as has been done in the case of many rheumatic patients.—G. M.

(**THYROID**) **Congenital familial goiter medically treated (Consideraciones sobre una observacion de bocio congenito familial tratado medicamente).** Brado (J.), Siglo méd. (Madrid), 1922, 69, 225-229.

Congenital goiter constitutes a rare clinical picture, the author having observed several cases in endemic regions among the children of those afflicted with goiter. These cases were sporadic, and, since goiter antecedents were absent, were of familial character. The author reports the cases of two females. One, two months old, had had a goiter since birth, which brought about asphyxial crises, hypotrophia (weight, 3,500 gm.) and dryness of the skin. After six months of thyroid treatment the general symptoms disappeared and the goiter was very much reduced. A sister, 11 years of age, weighed 35 kilos and presented a large goiter which had also manifested itself at birth. Three other sisters who died quite early in life also had goiters. The parents were syphilitic. The Wassermann test was positive, but the author does not believe syphilis to have been the cause of the goiter since the children showed no symptoms of hereditary lues and the specific treatment did not give results in any of the cases. Brado favors medical treatment of goiter and would use surgical treatment only when very intense signs of compression are present.—E. B.

(**THYROID**) **Exophthalmos in exophthalmic goiter; a study of 400 cases.** Bram (I.), Am. J. Ophth. (Chicago), 1922, 5, 609-622.

An illustrated résumé of the course, symptomatology and diagnosis of exophthalmic goiter with special reference to the exophthalmos. Exophthalmos and goiter are usually present, though they are no longer regarded as necessary constituents of the syndrome of exophthalmic goiter. Exophthalmos is rarely if ever the first sign of the disease, but it may be the first eye sign, if the patient presents eye signs at all. Occasionally, an inconstant von Graefe's sign will precede the appearance of proptosis, and more rarely a "hitch" on the downward descent of the upper lid may be observed. Though occasionally a patient will appear before his physician with exophthalmos as the only complaint, a careful examination will reveal the

presence of heart hurry, tremor, dermatographia, and other evidences of Graves' disease, which have developed prior to the exophthalmos, and which have occurred in such an insidious fashion as to have escaped the patient's attention. More or less insidiously, the exophthalmic patient is observed to become restless and emotional, there may be palpitation on slight exertion, a feeling of trembling and weakness in the lower limbs, excessive moisture of the skin, and a beginning of loss in weight. Soon it is noticed that when the patient enters into conversation or concentrates attention upon an object, the eyes present an unusual stare, a rim of sclera appearing above and below the cornea. Exophthalmos may occur only after the syndrome is fairly well advanced. It is in this class of patients, especially when there is an absence of thyroid enlargement, that the diagnosis is frequently belated, and the necessary treatment is attempted only after serious damage has occurred to the vital organs. Exophthalmos is accentuated during conversation, active attention, physical and mental excitation, menstruation, pregnancy, and fatigue. The 400 cases reported were seen by Bram during the years 1918 to 1921, inclusive. Exophthalmos may not be severe enough to occasion serious damage to the ocular mechanism. In most instances, the conjunctiva is somewhat congested, occasioning little or no discomfort to the patient. Vision, too, is uninfluenced. When eyes bulge markedly, the eyelids may close over the eyeballs with difficulty. Such patients commonly experience a burning sensation of the eyeballs, early fatigue of vision, excessive dryness or excessive moisture of the conjunctiva, and a varying grade of chronic conjunctivitis. In a small percentage of patients the exophthalmos is extreme, reaching the point at which the eyelids are incapable of coaptation. This frequently leads to corneal ulcers and opacities, with varying degrees of impairment of vision. In a few of Bram's patients, the habit of placing a small pad of gauze or flannel over each eye before retiring served as a protection against irritation during sleep. Unprotected eyeballs are a causal factor in the insomnia common to patients with Graves' disease. In an instance brought to the author's attention, the patient's exophthalmos was aggravated to the point of ocular dislocation by the administration on the part of an inexperienced attendant of 15 grains thyroid extract daily. Unilateral, then bilateral ophthalmitis developed, the subsequent panophthalmitis becoming so severe as to require a double eyeball enucleation in order to save the patient's life. Exophthalmos and thyroid swelling are the last signs of exophthalmic goiter to disappear during the course of successful treatment of the disease, indicating that the process of absorption of a pathologic redundancy of retroorbital fat, blood vessels, and other factors, real or hypothetic, is a very slow procedure. The facility with which this process occurs depends in large measure upon the previous duration and severity of the affection. The author came to the following conclusions. Exophthalmos

is probably the basis upon which all other eye signs commonly observed in Graves' disease depend. Exophthalmos in Graves' disease occurs somewhat more frequently in females than in males. Patients without goiter are less apt to present exophthalmos than those with a degree of thyroid enlargement. No definite general relation could be stated to exist between the degree of exophthalmos and the severity of the clinical syndrome. The symmetry or asymmetry of exophthalmos bears no relation to the symmetry or asymmetry of thyroid enlargement.—Author's Abst.

(THYROID) Acute afebrile myxedema (*Piccola epidemia di mixedema acuto afebrile*). Citelli (S.), Riv. ital. di neuropat. [etc.] (Catania), 1921, 14, 129-133.

(THYROID) Clinical experiences in 840 goiter operations, with special reference to recurrence of goiter and relapse operations (*Klinische Erfahrungen bei 840 Kropfoperationen, mit besonderer Berücksichtigung der Kropf-Recidive und Recidiv-Operationen*). Dubs (J.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 931-937.

This is only the concluding portion of the article. Injury to the sympathetic of the operated side occurred 4 times (about 0.4%). Dubs encountered 2 goiters, which entirely surrounded the trachea, and numerous substernal goiters. Exceptionally large goiters were often seen with the excised portions weighing from 600 to 800 gm. There were 11 cases of strumitis. Severe after-hemorrhage occurred 5 times (0.5%). Pneumonia following the operation occurred 15 times (1.7%), pleuritis once and lung abscess once. Tracheotomy during the operation was necessary three times. Ten deaths occurred (1.18% mortality). Of 255 patients recorded from 1914 to 1919 and personally investigated with reference to recurrences, 114 (44.7%) had had no recurrences at the beginning of 1922. Of the 141 (55.2%) with recurrences, 72 were accompanied by various complaints. The percentages of recurrences and non-recurrences for unilateral and for bilateral operations were about the same as for the whole group. The position of the recurrences following various types of unilateral operations is tabulated. Of these 63 out of the 98 recurrences were on the unoperated side. The other figures involve too few cases to be significant. Of the 74 cases with bilateral operation 39 had recurrences and 35 non-recurrences. The 255 cases are also tabulated so as to show the relative number of recurrences when different number of arteries were ligated. From 1914 to 1921 operations for recurrent goiters were performed on 53 patients (6% of total), 44 of them had a single recurrent operation, 7 had two recurrent operations and 1 had three recurrent operations. Tables also show the number of years intervening between the first operation and various recurrent operations. Eighty-four references are listed.—A. T. R.

Gastric ulcer of **THYROID** origin (*Úlcera de estomago de origen hipertiroideo*). Echeverría Martínez, An. fac. de méd. de Zaragoza, 1918-19, 235-246.

An article not amenable to abstracting, treating of a simple gastric ulcer which appeared coincidently with hyperthyroidism.
—E. B.

(**THYROID**) Intrathoracic goiter. Funk (E. H.), Progr. Med. (Phila. & N. Y.), 1921, 2, 307-312.

A review of the mechanical dangers of intrathoracic goiter, with implications of their urgent therapeutic indications. These goiters are rarely completely intrathoracic. The patient may state that there had been a goiter for years, but that it had disappeared or was "cured." But dyspnoea has remained, and the patient may be forced to assume certain positions in bed to prevent difficult breathing. An unconscious change from a favorable to an unfavorable position during the night may give rise to an attack of acute dyspnoea and coughing. On physical examination the patient is apt to hold the head high and stiff, or to bend the head forward. Percussion over the sternum gives rise to dullness, and auscultation reveals light, superficial breath sounds. The larynx may be in a state of ptosis, and its excursions during deglutition are reduced. Hoarseness calls for a laryngoscopic examination. Malignant intrathoracic goiter is rare. Exophthalmic goiter, with the cardinal symptoms, may also be intrathoracic in location. Mechanical goiter heart is the term applied to a confused, irregular, accelerated heart resulting from compression by an intrathoracic goiter upon the large vessels and nerves (especially the cardiac branches of the sympathetic nerve). A characteristic sign is the net of dilated veins on the neck and anterior upper chest. X-ray examinations are a great aid in diagnosis of intrathoracic goiters, especially in those rare instances in which there is suspected an enlargement of an aberrant thyroid. If, during deglutition in the fluoroscopic examination, the tumor follows the movement of the larynx and trachea regularly and synchronously, the diagnosis is assured. Surgical treatment is advised.—I. B.

HYPOTHYROIDISM. Funk (E. H.), Progr. Med. (Phila. & N. Y.), 1921, 2, 318-320.

Many cases of hypothyroidism are overlooked because they lack the classical picture of myxedema. The important symptoms are early obesity; mental symptoms; susceptibility to infections; hair anomalies; harsh, cold, atrophied skin; cold extremities; decreased temperature; and reduced size of the thyroid. Blood examinations and basal metabolism determinations are of great value, but are not absolutely reliable. Attention is called to hereditary hair and nail

defects as implying a tendency toward hypothyroidism. Cardiac dilatation, not amenable to heart tonics but to thyroid opotherapy, is common.—I. B.

(THYROID) Sporadic cretinism (infantile myxedema). Goldstein (H. I.), J. Med. Soc. N. Jersey (Newark), 1921, 18, 184-188.

A review of the etiology, symptomatology, classification, diagnosis, prognosis and treatment of sporadic cretinism, with reports of four cases which came under the author's observation. In three of the cases there was a prominent great toe, with a very wide space between it and the next toe. One grain of thyroid extract was administered two or three times a day. Within several weeks there was loss of weight, general improvement in appearance of the patient, increase in height, and a more normal mental life. This treatment may be supplemented by anti-leuitic treatment which seems to hasten results from the thyroid therapy. Kendall's thyroxin may also be employed. An excellent survey of the literature on the subject is appended.—I. B.

Deficiency diet and hormone activity. I. Effect of the reciprocal influence of deficiency diet and THYROID feeding on growth and development of tadpoles (Unzureichende Ernährung und Hormonwirkung. I. Über den Effect der gegenseitigen Beeinflussung unzureichender Ernährung und Schilddrüsenfütterung auf das Wachstum und die Entwicklung von Froschlarven). Groebbel's (F.), Ztschr. f. Biol. (München u. Leipz.), 1922, 75, 91-120.

Aqueous extract of thyroid inhibits the growth of *Rana temporaria* if applied during the spawning time; but in young tadpoles it stimulates the growth of gills. These effects increase with the protein content of the extract. Addition of acetic acid has no influence. Bouillon made from dog muscles and "biotose" inhibits the growth and development. Feeding of the tadpoles with only vitamin-poor "piscidin" accelerates the development more than the normal aqueous thyroid extract. Treatment of the animals with vitamin-poor thyroid piscidin delays development, especially of the hind legs. Restoration of sufficient food increases growth.

—Physiol. Abst., 7, 255.

(THYROID) Diathermic treatment of Graves' disease (Il trattamento della malattia di Basedow con la diatermia). Ghilarducci (F.), Atti assoc. rom. cultori elettr. e radiol. med., 1922, S. 2; abst., Rassegna internaz. di clin. e terap. (Napoli), 1922, 3, 326 (July).

On the basis of former experiments the author treated 3 cases of Graves' disease with diathermia to stop hypersecretion of the thyroid. In all 3 cases, after several sittings [from a minimum of 7 to a maximum of 25 sittings of 20 minutes each (1 to 1.5 A)], there was remarkable diminution of the size of the gland, the pulse

rate was decreased almost to normal and exophthalmos disappeared. The author believes that because the time of observation of the patients was too short we cannot as yet judge the real efficacy of the treatment, yet that the results thus far obtained are very encouraging and invite treatment on a larger scale.—G. V.

(THYROID) The influence of Wildbad hot springs water upon the forme fruste myxedema associated with endemic goiter (Ueber gunstige Beeinflussung der forme fruste von Myxoedema bei endemischen Kropfen durch die Wildbader Thermalwasser-Trinkkur). Grunow (W.), Klin.-therap. Wehnschr. (Berl.), 1921, 28, 105-113.

Ten cases are reported. A few presented a combination of Basedowian symptoms and myxedema, with a predominance of the latter. Drinking Wildbad hot springs water caused improvement in heart action, gastrointestinal function, psychic condition, and in the general appearance and sense of well being of the patient. There was an especially favorable influence upon the menstrual function. The spring water acted as a diuretic through a stimulation of metabolism. The author thinks that the influence of the water is somewhat akin to that of iodothylin and that in the presence of a degree of thyroid hyperplasia, there is material reduction in the bulk of the struma.—I. B.

(THYROID) Fermentative fluid contents of the duodenum in Basedow's disease. Gytoku (K.), Iji-Shimbun (Tokyo), 1922, No. 1091 (April).

In 60% of all the cases of exophthalmic goiter, the author states, there occurred a certain decrease in the fermentative fluid contents of the duodenum.—Jap. Med. World, 2, 297.

Respiratory gas exchange in struma vasculosa in childhood and after implantation of THYROID tissue in cretins (Ueber den respiratorischen Gaswechsel bei der Struma vasculosa im Kindesalter und nach Implantation von Kropfgewebe bei Kretinen). H'Doubler (F.), Schweiz. med. Wehnschr. (Basel), 1922, 52, 926-931.

In most cases the respiratory apparatus of Jaquet was used with the patient lying down. In some cases the head chamber of Grafe (as modified by Asher), with the patient sitting, was utilized. The oxygen consumption in the sitting position when compared with control determinations when lying down was in round numbers as 4 is to 3. The usual Haldane apparatus was used for the gas analysis. In three girls and one boy (all 13 years old) with pre-adolescent struma vasculosa (struma diffusa parenchymatosa, with great vascularity) and which might be classified as cases with thyrotoxic goiter hearts, but with no marked symptoms of hyperthyroid-

ism, the basal metabolism varied from +4% to -19% before operation and from -18.8% to -27% 3 to 8 months after operation. The resection reduced the basal metabolism on an average, 17%. In two other cases of moderate cretinism (13 and 16 years old) and one case of marked cretinism (35 years old) the average basal metabolism was -32%. Implantation of thyroid tissue produced no change in basal metabolism in two of the cretins and only a transitory increase in the third. The failure of the graft is attributed to the probable inactivity of the tissue (struma nodosa parenchymatosa) used. Some recent literature is listed.—A. T. R.

- (THYROID) Viscosity and protein content of the serum in Graves' disease (*Viskosität und Eiweißgehalt des Serums bei Thyreosen*). Hellwig, *Deutsche med. Wchnschr.* (Berl.), 1922, 48, 929.

In hypothyreosis the viscosity of the serum is increased; in hyperthyroidism it is diminished. After operation for hyperthyroidism the viscosity rapidly increases.—J. K.

Laryngological aspect of incipient HYPERTHYROIDISM. Hubert (L.), *Laryngoscope* (St. Louis), 1921, 31, 616-619.

Diagnosis is based upon the following symptoms: choking sensation, frequent colds, nervousness, palpitation on exertion, focal infections, tremor of the fingers and tongue, large pupils and tachycardia. Treatment consists of removal of focal infections, rest and diet. Quinin hydrobromate, 5 grains, t.i.d., acts like a specific in the early stages of hyperthyroidism.—H. W.

- The iodine content of the blood following THYROIDECTOMY. Hudson (W. A.), *J. Exper. M.* (Balt.), 1922, 36, 469-480.

The experiments recorded in this paper were undertaken to determine the relation of the thyroid to the iodine metabolism of the body, especially the effect of thyroidectomy on the iodine content of the blood. The author determined by Kendall's method the amount of iodine in the blood of 17 normal animals before and again some days after thyroidectomy. The average amount of iodine in the normal dogs was found to be 0.0079 mg. per 100 cc. blood. Blood examinations made from two days to two weeks after thyroidectomy showed very definite increases in the amount of iodine present. Administration of fresh sheep's thyroid by mouth caused the iodine content to fall again to the normal preoperative level. Discontinuation of the administration of thyroid led to a return of the blood iodine to the higher postoperative level.—I. M.

Effects of HYPOTHYROIDISM. Hutton (J. H.), *Illinois M. J.* (Oak Park), 1922, 42, 337-342.

An excellent review of the subject of thyroid deficiency. The author emphasizes the importance of heredity, especially on the

mother's side, as a factor in etiology. Most of the signs and symptoms depend upon deficient metabolism, not necessarily asserting itself in obesity, but often encountered in the poorly nourished, especially children. The entire chain of endocrine glands is involved in varying degrees. There is hypofunction of the pituitary, frequently enlargement of the thyroid from compensatory hypertrophy, uncertain dysfunction of the thymus, parathyroids and mammae, over-activity of the pancreas, hypofunction of the adrenals, and disturbance, probably hyperfunction, of the ovaries. The so-called thyro-ovarian syndrome is for the most part one of hypothyroidism. Headache, dizziness, hypertension, trophic disturbances of the skin, hair and nails, a feeling of chilliness, intestinal stasis, visceral ptosis, congestion and tenderness of the liver, tenderness of the gall bladder with a tendency toward cholelithiasis, albuminuria, and indicanuria are common. In children, nocturnal enuresis is observed. Milk teeth erupt late, their position is irregular, and the upper canines are markedly displaced anteriorly or posteriorly. In adults, pyorrhea is commonly observed.—I. B.

Acute yellow atrophy associated with HYPERTHYROIDISM. Kerr (W. J.) & Rusk (G. Y.), *Med. Clin. N. Am. (Phila.)*, 1922, 6, 445-459.

The patient was a farmer of 39 years. He entered the medical ward on October 27, 1921, complaining especially of weakness following influenza three years before. Acute symptoms of hyperthyroidism had been present for three months and a thyroid tumor had been noted for three weeks. Other complaints were nervousness, palpitation, tremor of hands and feet, weakness of the legs, increased perspiration, loss of weight, increased appetite, and polyuria. The physical examination revealed severe hyperthyroidism with a vascular thyroid tumor of moderate size. There was no exophthalmos. The heart showed moderate enlargement with good compensation. The blood-sugar curve showed decreased carbohydrate tolerance. The basal metabolic rate was markedly increased. There was a loss of 10.6 kilos in weight during the month in the hospital. Radium was inserted into the gland, with a probable slight reaction twelve days later. The patient left the hospital unimproved, to continue treatment at home temporarily. Three weeks later he returned to the hospital. During the first two weeks after discharge his weight fell to 47 kilos, and his appetite remained poor. Then improvement began with an increase in strength, appetite, and weight. The nervousness and other symptoms remained about the same. He still complained of marked constipation. There had been some local throat symptoms from the radium reaction, which were subsiding. During the first two weeks following readmission, there was marked improvement in the general condition, to the point that a bilateral partial lobectomy was

performed under gas and oxygen anesthesia, January 5, 1922. The patient began to vomit on January 16. This continued incessantly. Two days later, definite jaundice appeared, the patient became very much worse, with a marked increase in pulse rate, temperature, and respiration, and diminished liver dullness. There was bile in the urine. On January 20, the jaundice had become much deepened, the patient became semi-comatose, there were convulsive movements of the extremities, and after a sudden attack of dyspnoea, cyanosis, and rapidly failing pulse, the patient died. At autopsy performed two hours later, the liver showed almost complete loss of architecture, presenting the microscopic picture of acute yellow atrophy.

—I. B.

The respiratory exchange in HYPERTHYROIDISM. Technic of basal metabolism détermination (*Les échanges respiratoires des hyperthyroïdiens. Technique de la mesure du métabolisme basal*). Labbé (M.) & Stevenin (H.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, **46**, 1161-1163.

(THYROID) A case of adult myxedema and one of childhood myxedema. Lisser (H.), *Med. Clin. N. Am. (Phila.)*, 1922, **6**, 327-343.

The first case was that of a man of 38, with advanced myxedema of 15 years' duration. After treatment with thyroxin, he was so improved as to appear practically normal and to be able to resume his occupation as electrician. The second case was that of a girl of 14 with symptoms of hypothyroidism since birth, in whom marked improvement resulted from thyroid opotherapy. The author makes a plea for the prompt recognition of these cases so that treatment may be instituted early.—I. B.

La constipation THYROIDIENNE. Messerli (M.), *Rev. suisse de méd. (Berne, Lausanne)*, 1922, **22**, No. 13; abst., *Presse méd. (Par.)*, 1922, **30**, 750.

Messerli believes that constipation is a frequent ailment in patients with goiter and in cretins of certain Swiss districts. He attributes endemic goiter to an infection, the nature of which is undetermined, transmitted by water. This infection is favored by intestinal stagnation, and it is possible, by continuous laxative treatment, to obtain amelioration. Unlike Basedowian diarrhea, constipation is a well known symptom in myxedema, spontaneous or postoperative. Some constipation may be due to hypothyroidism, and judicious thyroid treatment sometimes helps the condition.

—R. G. H.

The history of the diseases of the THYROID and the development of its surgery. Moore (E. C.), *Southwest Med. (Phoenix)*, 1922, **6**, 319-325.

An interesting, general paper not amenable to abstracting.

—R. G. H.

(THYROID) Graves' disease (Basedowsche Krankheit). Neupert, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1221.

The right lobe of the goiter was removed, but recurred after some years. A second operation was performed and an arterial angioma racemosum of the other lobe was found. This condition is exceedingly rare.—J. K.

(THYROID) Can the disturbances of growth induced by lack of vitamine be influenced by chemically defined substances? (Kann die avitaminöse Wachstumsstörung durch chemisch definierte Substanzen beeinflusst werden?). Ogata (D.), Biochem. Ztschr. (Berl.), 1922, 132, 89-94.

Six groups of rats with 3 in each group were fed as follows. Group A was given a normal diet plus butter; group B, the same diet as group A plus NaI; group C, same diet as group A plus thyroid substance; group D, vitamine free diet of polished rice plus salt mixture; group E, same diet as group D plus NaI; group F, same diet as group D plus thyroid substance; 0.025 g. of NaI and 0.01 g. thyroid preparation was given for three rats on the basis of that amount per 100 gm. of rat weight. Notwithstanding the very small number of rats used in each group and the known variability of increments of weight of the rat, Ogata finds that as compared with group A all other groups were retarded in growth by the diets used.

—F. S. H.

Metabolic studies of two cases of constipation of THYROID origin (Estudios metabolimetricos sobre dos casos de estrenimiento de origen tiroideo). Oliver (P.), Arch. de méd. chir. y españ. (Madrid), 1922, 13, 607-620.

The existence of signs of thyroid insufficiency caused the author to think that this did not cause the constipation. This conclusion was proved by the metabolic determination (15% and 20% respectively). By employment of opotherapy the increased metabolism and constipation disappeared. In neither case was there hypo- or hyper-tonia of the nervous vegetative system; the author believed that the action of the thyroids on the intestines should be indirect, probably by catalytic regulation of all the functions.—E. B.

(THYROID) Strumous teratoma of the OVARY (Un caso di teratoma strumoso tiroideo dell' ovaio). Parodi (A.), Pathologica (Genova), 1922, 14, 572-578; 608-615 (September, October).

After a thorough review of all the published cases of thyroid teratoma, the author divides these tumors into two classes: the "pure," exclusively made of thyroid tissue with little or no ovarian tissue left, and the "false," formed of tissues originating from the various germinal layers plus some thyroid tissue. He claims that

the "pure" form, histologically as well as clinically, a very distinct class of ovarian tumors. Their size is nearly always uniform; there is no tendency to metastasis and either ovary may be invaded. Though as a rule they are found in women of over 40 years, some were found in women between 22 and 36 years of age. Ascites, which occurs very often, is not due to malignancy of the growth, nor to venous stasis, as in other ovarian and uterine tumors and which disappears after the removal of the tumors, but probably to hypersecretion of the constituent elements and rupture of the cysts into the peritoneum.—G. V.

(THYROID) Endemic goiter in Venezia, Lombardy and Emilia (*Ricerche sulla endemia gozzo-cretinica nelle regioni Veneto-Lombarde e nella provincia de Reggio Emilia*). Pighini, *Biochem. e terap. sper.* (Milan), 1921, 8, 12-16.

The paper is intended to call the attention of the Italian government to the need of an active and efficacious prophylaxis of goiter which, according to the views of the author, seems to be due to the condition of the drinking water.—G. V.

(THYROID) Relationship between histological structure and biological activeness of goiter tissue. de Quervain (F.), *Surg., Gynec. & Obst.* (Chicago), 1922, 34, 513-517 (April).

The author summarizes the present-day knowledge of the relationship between the histology and the function of the thyroid. He reports a series of experiments. Two rats were injected, one daily for 3 consecutive days with 2 ccm. of blood serum taken from an arm vein, the other similarly with thyroid venous blood. A third was fed for 3 days with a total of 60 gm. of tissue from the same struma. The experiments were made 31 times with blood from arm veins, 31 times with thyroid venous blood and 36 times with thyroid substances. Twenty-two common strumas, 4 Graves' strumas, and 8 cretin strumas were examined. It was found that feeding rats with goitrous substance always caused an increased sensitiveness to lack of oxygen. The strongest was found with exophthalmic goiters containing a little colloid, and then in decreasing order with non-toxic colloid goiter, general parenchymatous enlargement (adenomatosis according to Wilson), adenomatous goiters from non-cretins and from cretins. The injection of serum from thyroid veins produced in all cases a positive reaction, but less strong than did thyroid feeding. The order of succession was the same. The blood from veins of common goiters was distinctly more active than that of cretin goiters. Blood from the arm veins was distinctly active in the case of colloid goiter and parenchymatous enlargement, but this was not true in cases of adenomatous goiters, either from non-cretins or cretins. In three out of four cases of dwarf cretinism with thyroid atrophy (without goiter) the blood from the arm produced a decrease in the sensitiveness to lack of oxygen.—E. N.

Respiratory gas exchange in struma vasculosa in childhood and after implantation of **THYROID** tissue in cretins (Ueber den respiratorischen Gaswechsel bei der Struma vasculosa im Kindesalter und nach Implantation von Kropfgewebe bei Kretinen). de Quervain (F.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 925-926.

A brief discussion of the types of apparatus used in the determination of gaseous exchange and the importance of basal metabolism in thyroid disturbances.—A. T. R.

(**THYROID**) Rudimentary development of the left lobe with goiter of the right (Rudimentäre Entwicklung der linken, bei Kropf der rechten Schilddrüsenhälfte). Rohde (C.), Klin. Wchnschr. (Berl.), 1922, 1, 1738-1740.

In the literature 7 cases have been described of absence of one lobe of the thyroid. The author describes the remarkable cases of two brothers. Both had a partly colloid and partly parenchymatous goiter of the right lobe and the left lobe was about the size of a cherry stone. In both patients the right lobe was removed with good results. Diagnosis was made only after the operation.—J. K.

(**THYROID**) Goiter—with an analysis of one hundred operated cases. Rowley (A. M.), Boston M. & S. J., 1921, 184, 486-489.

There is no apparent relation between goiter, heredity, focal infections and occupations. Of the 100 cases, 91 were in women and 9 in men. Among the women, goiter followed excessive hypertrophy at the period of adolescence in 14 and followed pregnancy in 8. Five patients lived in goiter districts; no etiology was recognized for the remaining number. The youngest patient, 12½ years old, had a hyperplastic goiter; the oldest, 66 years old, had a toxic adenomatous goiter. The average length of time for development was 3 years, 9 months, the longest was 20 years and shortest 3 months.—H. W.

A new substance extracted from the **THYROID** (Ueber einen neuen Extraktivstoff aus der Thyroidea). Sammartino (U.), Biochem. Ztschr. (Berl.), 1922, 132, 293-294.

A technical description of the method of isolation of a compound of indefinite composition, the physiological action of which is unknown.—F. S. H.

THYROID and fluid exchange. Intravenous saline and oral water administration in rabbits before and after **THYROIDECTOMY** (Schilddrüse und Flüssigkeitsaustausch. Beobachtungen hierzu bei intravenösen Kochsalzfusionen und Wassergaben per os bei Kaninchen vor und nach Entfernung der Schilddrüse). Schaal (H.), Biochem. Ztschr. (Berl.), 1922, 132, 295-308.

No alterations in the course of the NaCl and dry matter changes of the blood in diuresis induced by intravenous injection of NaCl solutions were obtained by thyroid feeding or removal. Diuresis induced by oral ingestion of water was similar in rabbits to that in dogs as found by Eppinger (Zur. pathol. u. therap. des menschl. Oedems, Springer, 1917) after thyroid feeding or removal. The influence of the diet, particularly drinking, is so strong that previously "desiccated" animals show a different course of fluid exchange from the normal. Hemoglobin, as a measure of water content, is of value only in severe experimentation such as blood-letting. It is concluded that the thyroid is effective in water exchange and diuresis only when its tissue activity is concerned. If alterations in swelling pressure of protein have to do with the fluid exchange through mediation of the thyroid, it is accomplished primarily through tissue action. The action of the thyroid on the blood protein is apparently not sufficient to influence fluid exchange in the living animal.

—F. S. H.

Cystic goiter: THYROIDECTOMY under local anesthesia. Skillern (P. G.), Internat. Clin. (Phila.), 1921, 31, 63-66.

Report of a case and description of technic employed.—I. B.

On errors of refraction in HYPERTHYROIDISM. Sourasky (A.), Lancet (Lond.), 1922, ii, 611-612.

The author reports the refraction errors in 20 patients with hyperthyroidism, 16 of whom had exophthalmos of varying degrees. In the 16 cases (32 eyes) with exophthalmos the disturbances were distributed as follows: hypermetropia, 1; simple hypermetropic astigmatism, 1, compound, 13; myopia, 2; simple myopic astigmatism, 7, compound, 5; mixed astigmatism, 3; i. e., 29 out of 32 eyes had astigmatism, 14 had hypermetropic astigmatism and 12 myopic astigmatism. This is a higher incidence of astigmatism than is usually found and the proportion of myopic to hypermetropic astigmatism is increased. In the 4 cases (8 eyes) of hyperthyroidism without exophthalmos the distribution was: compound hypermetropic astigmatism, 6; compound myopic astigmatism, 1; myopia, 1. While in some cases the errors noted may be dependent in part upon the changed position of the eyeball, it is not clear whether this may be a general manifestation. Headache was present in a large percentage of the cases. This was relieved by the use of properly fitted glasses. There was a general improvement in the patient's condition in many cases.—I. M.

(THYROID) Graves' disease; diagnosis and prognosis (Morbus Basedowi; diagnostiska och prognostiska synpunkter). Troell (A.), Svenska Läk. Handl. (Stockholm), 1922, 48, 1-23.

During the past 2 years the author has operated upon 26 cases of thyroid adenoma with hyperthyroidism and 20 cases of diffuse

exophthalmic goiter. The patients belonging to the first group had suffered from symptoms for 14 years on an average, and those belonging to the second group for 5 years. Most cases of definite Graves' disease were found in this group. The diffuse goiter as a rule showed an increased blood pressure and a decreased sugar tolerance. The adrenalin test (Goetsch) gave a positive reaction in 85% of the cases of hyperthyroidism; atoxic goiter showed positive reaction is only 15% of the cases. Injections of pilocarpin and pituitrin had no diagnostic value since patients with toxic goiter did not react differently from healthy persons. Cases with diffuse goiter and a high blood pressure proved to be grave.—H. B.

(THYROID) Anatomy of goiter especially in Graves' disease (Omstrumans byggnad med särskild hänsyn till Morbus Basedowi). Troell (A.), Svenska Läk. Handl. (Stockholm), 1922, 48, 125-166.

The author has studied 21 cases of diffuse toxic goiter, 27 cases of adenomatous toxic goiter, 4 cases of atoxic diffuse goiter, and finally 10 cases of atoxic adenomatous goiter. He comes to the conclusion that 50% of the cases of toxic goiter show characteristic anatomical changes. Besides the previously well known changes of the acini and the parenchyma cells in shape and size, he describes a difference between the toxic and atoxic goiter in the aspect of the inner end of the cells. The former shows Heidenhain's border lines; the later does not. To demonstrate the changes of the colloid he has fixed the glands in Susa's fluid and used Heidenhain's combination of azocarmin and Mallory's stain. The colloid then generally became blue in toxic and red in atoxic goiter. According to the author the microscopical aspect of toxic goiter is so characteristic that it is possible in many cases to diagnose the disease simply by examining microscopical sections.—H. B.

(THYROID) The effect of iodine and iodothyrene on the larvae of salamanders III. Uhlenhuth (E.), Biol. Bull. (Woods Hole), 1922, 42, 143-152.

Nine axolotl larvae of *Ambystoma tigrinum* were employed. Three were used as controls, three were fed iodothyrene and three inorganic iodine in known amounts. A dose of iodothyrene containing only 0.03 mgm. iodine per liter of water caused metamorphosis in 13 days. Inorganic iodine in amounts 33 to 86 times greater, and feeding even larger doses directly by mouth, did not cause metamorphosis. The author concludes that amphibian metamorphosis is truly the expression of thyroid activity and not the result of the effect of inorganic iodine, and that inorganic iodine as such is not the active principle of the thyroid hormone.—W. J. A.

A study of the distribution of iodine between cells and colloid in the THYROID gland. IV. The distribution of iodine in the hyper-

plastic **THYROID** gland of the dog after the intravenous injection of iodine compounds. Van Dyke (H. B.), J. Biol. Chem. (Balt.), 1922, 54, 11-18.

The findings of Marine and Feiss, and Marine and Rogoff that the hyperplastic thyroid gland of the dog rapidly binds iodine intravenously introduced as a solution of KI were confirmed. By a method already described the ratio value of iodine in the cells to iodine in the whole gland was determined and found to be very low after the intravenous injection of KI solution into dogs with hyperplastic glands when these glands were removed 1.5 to 60 minutes after injection. The ratio value more nearly approached the normal if the interval elapsing was made about 24 hours. This finding is in keeping with the histological changes described by Marine and Rogoff. When iodine as colloid iodine solution of normal animals was given intravenously practically none of the colloid iodine was taken up by the hyperplastic glands during the periods of times used in these experiments. The incompletely synthesized principle is probably more diffusible and more readily split into simpler products than active principle fully formed.—F. S. H.

THYROID insufficiency and sterility (*Insuffisance thyroïdienne et stérilité*). Vignes (H.) & Cornil (L.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 850-852.

Total or subtotal suppression of the thyroid body is accompanied by an infantile condition of the genital organs, amenorrhea and sterility. A less accentuated insufficiency gives rise to menorrhagia. These may be the principal clinical signs of hypothyroidism. The nature of the sterility is discussed and a clinical case described.

—T. C. B.

THYROID insufficiency and sterility (*Insuffisance thyroïdienne et stérilité*). Vignes (H.) & Cornil (L.), Progrès méd. (Par.), 1922, 37, 283-284.

A case report which the authors believe demonstrates the production of sterility from hypothyroidism. The patient was a woman of 32 years, who had typhoid fever at 11 years. She menstruated also at 11. She was married at 24, but was sterile up to the age of 31. At that time she underwent treatment with iodine for obesity and became pregnant. She aborted after 2 months. She has the physical appearance of a person with hypothyroidism. A second gestation occurred after the reinception of the iodine treatment. This pregnancy was also threatened by abortion, which was averted through medication with thyroid extract. There were gynecological symptoms of an endometritis which were not confirmed by histological study of the tissues at delivery. It is therefore inferred that the sterility observed before treatment with iodine and thyroid was due to the influence of the lack of the thyroid secretion on the reproductive functions.—F. S. H.

(**THYROID**) Hypo- and a-thyreosis and blood picture (Hypo- und Athyreosis und Blutbild). Wälcchli (E.), *Folia hæmatol.* (Lelpz.), 1922, 27, 135-140.

The only constant change in the blood in endemic cretinism is a hastened coagulation time. The number of erythrocytes is often low, while the hemoglobin content is normal and the color index high. In many cases the total number of leucocytes is high.

—J. K.

(**THYROID**) The surgical treatment of goiter. Wathen (J. R.), *Kentucky M. J.* (Bowling Green), 1922, 20, 168-174.

Cystic and adenomatous goiters should be operated upon before they become so large as to encroach upon the trachea or before they degenerate into toxic types.—H. W.

The mental side of **HYPERTHYROIDISM**. Weinberg (M. H.), *Penn. M. J.* (Harrisburg), 1922, 25, 618-624.

The author contends that mental symptoms usually appear early in Graves' disease, frequently long before the classical eye changes and marked cardiovascular signs develop. This mental syndrome consists of restlessness, anxiety, indecision of will, depression, apprehension, irritability, timidity, etc. Beckley and Follis go further and consider catatonia to be due to perverted thyroid secretion, and apparently found marked improvement following partial thyroidectomy. Weinberg described briefly the various types of mental disturbances seen in thyrotoxicosis, such as paranoid, dementia præcox, and the very severe acute toxic type. Several case histories are presented illustrative of these types. (No basal metabolic rates are given, and the meagerness of the ordinary, accepted symptoms and signs of toxic thyroids led several who discussed the paper to express some doubt about the thyroid origin of the mental abnormalities described.)—H. L.

On the relation of the **THYROID** gland to the female pelvic organs. Wilson (C. M.) & Bourne (A. W.), *Lancet* (Lond.), 1922, i, 1038-1043.

The object of the investigation presented in this paper was to study the function of the thyroid gland by determination of the basal metabolic rate during pregnancy and in the condition of functional menorrhagia. It was found that the basal metabolic rate was increased in the majority of pregnant women. There was no definite correspondence between the rate and the clinical condition of the mother or child. In the majority of cases it returned to normal after the puerperium. It was not clear whether the increased rate was due to the maternal thyroid overactivity or to the foetal metabolism being added to the maternal. In some of the cases with persistence of increased metabolic rate after the puerperium menor-

rhagia persisted without pelvic disturbances sufficient to explain it. In such cases Roentgen radiation of the thyroid gland reduced the basal metabolic rate to normal and at the same time menorrhagia disappeared.—I. M.

(THYROID) A case of lingual goiter (*Ein Fall von Zungenstruma*). Zehner (K.), München. med. Wchnschr., 1922, 69, 747-748.

A severe fright of a woman of thirty was followed by a tumor in the mouth. A part of the tumor was removed. It proved to be a cystic, colloid struma of the tongue. No other thyroid was found in its classical place.—J. K.

(THYROID) Local adiposity in Graves' disease (*Lokalisierte Fettsucht bei Morbus Basedowi*). Zondek (H.), Klin. Wchnschr. (Berl.), 1922, 1, 444.

The patient was very cachectic; operation was not successful. In the lower part of the body, however, there was a great deal of subcutaneous fat. The respiratory metabolism was increased. The same symptoms were found in another patient. This makes it probable that in this local adiposity a nervous influence plays a role, independent of the general metabolism.—J. K.

(VERMIFORM APPENDIX) El apendice ileo-cecal como glandula endocrina. Perera, Progr. clin. (Madrid), 9, 525-531 (May).

A review of the endocrine functions attributed to the vermiform appendix and an exposition of personal experiences which induce the author to consider that it has an internal secretion which regulates the gastro intestinal motility. The author discusses certain cases which recurred after appendicular opotherapy.—G. M.

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THE PINEAL GLAND, ESPECIALLY IN RELATION TO
THE PROBLEM ON ITS SUPPOSED SIGNIFICANCE
IN SEXUAL DEVELOPMENT

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The pineal gland, glandula pinealis, corpus pineale, epiphysis cerebri or conarium is an organ, the function of which has remained unknown up to the present day. Correlated with this lack of knowledge is the fact that the organ has been the subject of the most various theories. During a philosophical and speculative period this centrally situated organ was considered to be the seat of central psychic activity. At a later period, the "acervulus cerebri" contained within the organ, which apparently always attracted attention, was for this reason considered as very important. Later, it was learned that this organ is homologous with the pineal eye in lower forms and it was relegated to the status of a rudimentary organ without any significance at all. Still later, the observation of a connection between tumors in the pineal gland and precocious development in the genital sphere opened the eyes of authors to the possibility of the pineals being an incretory gland and various observers who performed experiments upon animals have, in the opinion of many, supported this hypothesis. In a period in which the study of the internal secretions has seen, more than ever, days of full bloom, many technical faults have been committed in the investigations. In the studies on the pineal gland, one has very



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often the impression that the authors' desire to consider the organ as incretory in function is greater than their critical judgment regarding published researches. There is a priori no justification for entertaining such a desire or even the opposite.

In the following pages, I shall give a report of our present knowledge of the pineal gland and show what conclusions as to its function may justifiably be inferred. In each aspect of the problem we shall try to evaluate the arguments pro and con. Although I must confess at once that I do not share the prevailing opinion, though it may possibly be true, that the pineal gland exerts an influence on sexual development, I consider it sufficiently demonstrated that in most mammals, including man, the pineal gland is not at all rudimentary, but that it probably has an incretory function. Finally, it seems probable that future investigations will result in technique more fruitful than special study of the relations of the pineal to sexual development. It is to be hoped that investigations of its relations to the cerebro-spinal fluid and to brain metabolism will receive more adequate study than heretofore.

COMPARATIVE ANATOMY

In Inferior Vertebrates and Birds

Details as regards these groups may be found in the monographs of Studnicka and of Tilney and Warren. We may only mention that while the pineal gland has not been found in the lowest vertebrate, the amphioxus lanceolatus, it has been demonstrated, with some exceptions (as in crocodiles and edentates), in all vertebrates that have been examined from the lamprey up to the man. In the lamprey, it is a structure resembling an eye. In the higher fishes it is a sacciform structure, the walls of which sometimes resemble glands. In the urodelian batracians, the pineal gland is a simple pouch; in the anurodeles the distal part bears analogy to an eye situated beneath the skin, but the proximal part resembles a gland. In reptiles the gland is sometimes sacciform, sometimes analogous to a gland in its structure, chiefly in snakes, whose type comes near to the mammals. In birds, the organ is formed by a group of isolated follicles. Altogether the organ in the vertebrates varies from an eye-like formation to a gland-like element.

In front of the pineal gland, there exists in quite a number

of inferior vertebrates another element, the parietal eye, which is already found in the lamprey and which, in the saurians, is developed into a typical eye-like formation. In the superior vertebrates, this organ disappears or is rudimentary.

Comparative Embryology and Anatomy in Mammals

For details the reader is referred to two previous articles which I have written upon the same subject (63, 64). On the whole, the pineal gland shows, during fetal life as well as during the period of youth, a constantly progressive and augmentative development which, at the same time, implies a differentiation. It is only in the edentates that the pineal gland totally disappears; in whales it is rudimentary and in the manatees it may possibly be absent, but in all other mammals that have been investigated it presents such a characteristic development that it seems absolutely unjustifiable to call it a rudimentary organ. In the rodents, during fetal life, the exterior form is tube-like; in the adult rodents it has the form of a club or of a thread. In the most of other mammals, the pineal gland, during fetal life, has the form of a pouch or of a button; in the adults it has generally the form of a pea or of a bean. In some (rabbits and swine) the follicular structure exists in fetal life, during a transitional period, but it disappears again; it is only in the inferior mammals, didelphys, and in the elephants, that follicles are found in the walls in the adults. In full-grown mammals the organ is principally formed of a uniformly constructed parenchyma, whose main mass is formed of a specific cell-type; among the pineal cells, proper, exists a small quantity of neuroglia cells, in the superior apes (as also in the man), there are also nerve cells. In most mammals there are found an abundant quantity of nerve fibres. In the horse, swine (and also in man) we find a connective stroma in the parenchyma. In old horses and oxen there are sometimes to be found calcareous concretions. Ordinarily the organ is very vascular; this is especially true in some classes of seals. Pigment exists abundantly in the ass.

Structure of the Pineal Gland in Man

In the course of fetal life, the organ develops from two anlagen, a sacciform one and another in form of a button; at a later period they coalesce. In children and adults, the pineal gland consists of parenchyma and of trabeculae of connective

tissue. In the parenchyma, the pineal cells form the main mass and assume peculiar conditions in adults. There are seen numerous amitotic cell division and a great number of processes of "nucleus excretion." Neuroglia cells are found in a number corresponding to that observed in other parts of the central nervous system. Nerve cells are seen in larger quantities than in any other mammal; they send offshoots which end in dense bundles of button-like swellings. [However, some authors (57) do not admit the existence of nerve cells.] The partitions of connective tissue develop in the first year of life and increase in number in after-life. Nevertheless, we may find in old people connective tissue conspicuous by its scarcity and a large quantity of parenchyma is always preserved into advanced age.

After the age of 8 years (very seldom before) there exists a more or less large proportion of calcareous deposits, and oftentimes small cysts. In the connective tissue, quite a number of *mastzellen* and of scavenger cells are to be found.

What Conclusions About the Function of the Pineal Gland Can We Draw from the Anatomical Conditions of the Organ?

It must be considered as very probable that the pineal gland, in man and in most mammals, is not a rudimentary organ; the term meaning an organ which, in an earlier phylogenetic stage, had a function, but which, at the present time, is without function, the organ retaining the form of the previous stages, but now composed of indifferent supporting tissue (connective tissue, cartilage, fibrillar neuroglia). The pineal gland can then be considered as rudimentary only in the edentates, the whales and possibly the manatee. In the opossums and elephants, it must be considered as scarcely developed, but not rudimentary in the true sense of the word. The arguments in favor of the opinion that the pineal gland is not rudimentary in most mammals are the following. From first stages of fetal life until youth, the pineal gland undergoes an increase in size. It is formed of a specific and much differentiated tissue. It is very vascular. In its structure, the pineal gland usually differs considerably from the gland of a few mammals in which it is rudimentary. The conditions which have been taken as indicating its rudimentary state are the following. (1) The organ at a previous stage of the phylogenetic development has probably been an eye. But this proves nothing; it proves at most that the peripheral part

of the organ can be considered as rudimentary. With reference to the central part, there can be only a question of discontinuance of its function, but not of its rudimentary state. (2) There are found certain concretions. These deposits are also found in the membranes of the brain, but without these being necessarily considered as rudimentary organs. (3) Plates of neuroglia are found in man. However, these cannot be viewed in the sense of a destruction of tissue, but as remnants of the diverticulum which exists in fetal life.

As to the function in mammals, it is not impossible that there can exist some variations. Thus it is a striking fact that in the majority of ungulates the organ has the hardness of cartilage and is chiefly formed of fibrillar neuroglia. It is also possible that this condition may be the expression of a beginning rudimentary state. The considerable vascularization in the seals is also a variation which could indicate peculiarities in the function. Lastly, the development of the large quantity of nerve cells in man and in the higher apes is a condition which could be interpreted in the sense of an advance in the functions.

The next question to be answered is, What is the nature of that function? The first which comes into consideration is a glandular function. The arguments favoring such a function are as follows: as a whole the organ is rather like an endocrine gland; the organ is considerably vascularized; there exist numerous amitoses. Possibly the process of nucleus extrusion in man is the expression of a glandular function, but this is not at all certain. To conclude, we must remark that the glandular function has its ontogenetic analogy, because the ependyma of the choroidal plexus, which, like the pineal gland, is developed from the ependyma of the cerebral ventricles, is supposed to possess a glandular function.

If we consider, on the other hand, the arguments which could be produced against a glandular function, they center in the important objection that the protoplasm (with the exception of the hedge-hog) is extraordinarily scarce and that in mammals it does not contain granulations which ought to be considered very probably as secretory (here we except the granulations which in man are evacuated from the nuclei into the protoplasm). Nevertheless, this is not a definite proof against a secretory activity. On the contrary, that could probably indi-

cate the possibility that, in an eventual secretory activity, we have to do not with a secretion of albuminous or lipid substances, but rather with a secretion of salts and eventually with a regulation of the concentration of hydrogen-ions or with similar processes. The presence of a large quantity of nerve cells in man does not speak against the secretory activity, because we observe quite the same phenomenon in the medullary portion of the adrenals. At the most, that could be the manifestation of the fact that, in man, there is an advance in function which is not already completely accomplished and which is in being. It is only in ungulates that it must be considered as doubtful if there really exists any secretory function, because the organ has wandered far away from the glandular type and consists chiefly of fibrillar neuroglia.

Must this (eventually secretory) function be supposed to last throughout the entire life? The answer to this question must be decisively affirmative. In an advanced age we see, it is true, some atrophy of the organ, but not more than in the other organs. There can be no question of any suppression of the function in man after puberty because, after this period, a predominant quantity of specific tissue remains in the pineal as contradistinguished from what it does, for example, in the thymus.

Could we from the histological structure draw any conclusions with reference to the nature of the eventual secretory function? The answer to that question must be negative. It will seem, beforehand, natural to admit that an organ so intimately connected with the brain and, which on all sides, is surrounded by cerebro-spinal fluid, plays a special part in the metabolism of the brain and of the cerebro-spinal fluid. This is also an hypothesis for the sake of investigation which ought to be considered more than it has been hitherto the case. But we do not have any proof that the conditions are really such.

Could we perhaps draw any conclusions from the rudimentary or undeveloped state of the organ in certain animals (edentates, whales, possibly manatee and, partly, elephants)? There are also many difficulties. In these animals, one will find such a considerable reduction in the organs (teeth, hair, genital organs) in so many and such different locations and in no lesser degree in the entire brain, that one must view this reduction of

the pineal gland only as a link in the general reduction. Farther, one must consider the possibility that in these animals another organ could have taken up the function of the pineal gland [cf. the demonstration by Broman (297) of an endocrine gland in the snout of the dasypus].

If we do not take into consideration the possible significance of the fact that it is proved that the organ has disappeared in these animals or is considerably reduced, one must be very cautious in drawing conclusions from the size of an organ as to the importance of its function. For instance, the pineal gland is relatively large in sheep, but is formed chiefly of fibrillar neuroglia. If we suppose that the eventual secretory function is connected with the pineal cells we should infer that the gland has a far more important function in carnivora, whose pineal gland is small, but consists chiefly only of pineal cells, than in sheep, in which that gland is large. However, many authors have in a faulty manner reversed the conclusion.

PATHOLOGICAL ANATOMY

The pathological changes which are the most frequently described in the pineal gland of man are tumors, which take up the site of the gland, and, in some cases, in such manner that the tumor has completely destroyed the pineal gland, and in other cases, a portion of the tissue is preserved either as a delicate coating around the tumor or in form of normal, slightly modified, pineal tissue as basis for the neoplasm.

The nature of the tumors has been various. In about the half of the cases they were sarcomata. Some of the cases have been gliomata. The denomination of carcinoma for some of the tumors is unjustifiable. That applies also to a case which has been described as an adenoma. About one-fourth of the described tumors were teratomata. This condition presents great interest, as it is striking that a tumor so rare as teratoma grows in so large a percentage in the pineal gland.

The presence of teratomata in the pineal gland can best be explained as a precocious development in fetal life. During the course of intra-uterine life, the germ of the gland, in man and in many other higher animals, comes very near the surface, nearer than any other part of the brain; for this reason, there are, to a superlative degree, conditions facilitating penetration of the elements of foreign tissue into the organ and, in that

manner, forming the starting point for these peculiar tumor formations. The incidence of teratomata is to be easily explained in this way. Nicolas and Dimitrova found in the oxen transversely striated musculature in the distal part of the pineal gland. This apparent freak, the presence of isolated muscular bundles in a part where it is difficult to assign them any function, must probably be explained in a corresponding manner as being the penetration of tissue coming from the surface. The same will apply also to the tumor described by Pappenheimer, in which quite a number of muscular fibres did exist. In a single case (Askanazy) which presents the structure of a chorioepithelioma, one must assume that the chorionic epithelium has been, in an analogous manner, drawn into the organ. However, other authors deny that the tumor was a real chorioepithelioma.

Among other tumors which present a special interest, we may mention Ogle's case of melanosarcoma in the pineal gland.

In quite a number of cases termed psammosarcomata, a number of corpora arenacea has been found. That must be viewed in natural relationship to the fact that corpora arenacea are found not only in the pineal gland, but also in the membranes of the brain; thus it cannot be brought forward as a proof that the tumor arises precisely from the specific tissue of the pineal gland.

Metastatic tumors have been found twice (Förster, Jacobi); these were a carcinoma and a sarcoma. Other pathological conditions different from tumors have been rarely described. Total absence of the pineal gland in man has been mentioned by some authors, but it cannot be considered as quite established, because when the brain is taken away from the cranium, the pineal gland becomes oftentimes detached, as the organ remains hanging by the vena magna Galeni; it is very probable that such has been the case in the reported instances of absence of the gland. I was afforded the opportunity of investigating a case in which there seemed to exist a total absence of the pineal gland. The case was that of a female infant, one year old, with considerable hydrocephalus. Serial sections through the region of pineal gland showed that the organ was transformed into a pouch of neuroglia with thin walls, without any sign of pineal cells. The infant did not present any remarkable symptoms except its hydrocephalus and, especially, no precocious puberty occurred.

The formation of cysts has been described sometimes. As mentioned above, there normally exist small cysts in the pineal gland and their size can vary in marked degree. I have myself seen twice, as casual post-mortem findings, cysts of the pineal gland. It seems that they did not cause any symptom. A single case of symptom-producing cyst is described in the literature; the cyst by its pressure has flattened the aqueduct of Sylvius. But it seems rather that this case was one of tumor with cystic formation.

Lord describes a case of syphilitic enlargement; however, there is no decisive proof that this process was really of syphilitic nature. In Pontoppidan's case, it was doubtful whether the tumor was a round-cell sarcoma or a gumma. Besides, the syphilitic process may of course invade the pineal gland as well as the other organs. I observed an example of this kind (and later did Josephy) in dementia paralytica, where the walls of the vessels in the pineal gland as well as in the rest of the brain were infiltrated by plasma cells.

In tuberculous meningitis, also, I have seen the tuberculous process involving the pineal gland. But, for the rest, concerning all that is termed atrophy, hypertrophy, fibrous changes and cystic formation in the pineal gland, we ought to stand on the reserve, because the limits for the normal findings are particularly broad precisely in the organ we speak of.

Atrophy and sclerosis in the pineal gland are described very frequently. As mentioned before, in advanced age there appears very often a slight atrophy of the organ running parallel with the atrophic senile changes in the other organs, but these changes must not be regarded as an involution of the organ. The quantity of connective tissue may vary considerably, so that the denomination of a "cirrhosis" of the organ should be taken into consideration with all possible reserves. I have seen twice, in children, an enormous development of connective tissue; one of these was a girl, aged 12, who died of osteomyelitis, but she had not presented any remarkable symptoms; the second was a subject of tuberous sclerosis of the brain associated with precocious puberty. This case is reported in "L'Encéphale" (299).

CLINICAL SYMPTOMS RELATED TO THE PINEAL GLAND

Practically speaking, the symptoms which are found in the tumors of the pineal gland can be divided in three principal

groups: (1) General brain symptoms; (2) Symptoms from the neighboring parts of the cerebrum; (3) Dysendocrin symptoms.

On the whole, the general brain symptoms are of the same character as in other cases of cerebral tumors: headache, vertigo, drowsiness, which merges into coma, neuritis optica, which can pass on to atrophy and amaurosis, vomiting and attacks of general convulsions, coma, and finally death. The development and the course of the symptoms nevertheless in some degree depend upon the region in which the organ is situated; the growing tumor very soon produces closing of the aqueduct of Sylvius and in this way a considerable hydrocephalus internus (which is nearly always found at autopsy). For this reason, we observe, at times, a conspicuously rapid development of the symptoms and often a short course from the beginning of symptoms until death. Besides, none of aforesaid symptoms is absolutely constant; even the optic neuritis disc is absent in some cases. Considerable drowsiness is a peculiarly constant symptom and, as this phenomenon, as well as the paralysis of the ocular muscles, are predominant in the clinical picture, the differential diagnosis from lethargic encephalitis presents several difficulties.

The symptoms from neighboring organs are primarily symptoms from the nuclei of the ocular muscles and from the tracts in the corpora quadrigemina. In this category, the palsies of the ocular muscles are also very frequent symptoms. They can be attributed in part to a palsy of the abducens, which may be considered in the light of a general symptom of brain compression. However, there have been observed in a series of cases indubitable palsies of the oculo-motor and of the trochlearis without palsy of the sixth nerve. The other localized symptoms from the brain must rather be considered as distant symptoms. There has been observed palsy of the facial nerve and of the extremities, on one side or on both, hemianesthesia, hemiataxia and tremor, forced position of the head and of the eyes, nystagmus and, in some cases, deafness. As a whole, these symptoms do not present anything characteristic. The palsies of the ocular muscles have only, properly speaking, importance for the diagnosis. When they appear at an early stage of the disease and are much marked in comparison with the other symptoms from the brain, they should direct attention to a localization of a

tumor in the region of the corpora quadrigemina, *i. e.*, in the pineal gland or in its immediate vicinity.

The dysendocrine symptoms can for a considerable part be regarded as pituitary (or infundibular) symptoms. That applies very probably to the adiposity, which has been described in at least 8 cases (Marburg, Bailey and Jelliffe, Schmidt, Nothnagel, Müller, Daly, Kny, Löwenthal) and perhaps some others. Furthermore, in some cases, polyuria has been observed. Since these symptoms, as we know, are found very frequently encountered in diseases of the pituitary body (without complicating disturbance of the pineal gland) and since, in a number of cases, the pituitary body has been found flattened by the increased cerebral pressure, there is no little reason to consider these symptoms as distant pituitary symptoms and not as pineal symptoms. Whether these symptoms are due to pituitary disturbances or to deranged function of mesencephalic centers is an interesting problem, but outside the scope of this paper.

The cases in which complication with affections of other endocrine or possibly endocrine glands has been observed occupy a very remarkable situation. That applies, for instance, to the Case I of Neumann in which the thyroid gland was considerably enlarged, the thymus large and lobulated; also to the cases of Christ, in which existed a struma gelatinosa totalis and hyperplasia of the thymus, and of Raymond-Claude, in which small adenomata were found in the cortical portion of the adrenals, and to the case of Goldzieher, in which the adrenals were hyperplastic. We cannot determine of a certainty whether in these cases, we have to deal with secondary phenomena or with coincident anomalies.

Lastly, we come now to the well known cases in which there had been precocious development of secondary sex characters or of the body as a whole. In the year 1883, Henrot described a case in which there was a concomitance of acromegalic gigantism and of sarcomatous tumor both in the pituitary body and in the pineal gland. Gutzeit (1896) observed a teratoma in the pineal gland complicated with considerable development of pubic hair in a boy of 7 years and 3 months. Huebner and Oestreich-Slawyk, who have separately reported the same cases, have found in a boy of 4 years with a so-called psammosarcoma (afterwards it was recognized as a teratoma—Askanazy) in the

develop after injection of fetuses reduced to pulp (Starling), some authors have succeeded in accelerating pregnancy, *i. e.*, the secretion of substances from teratomata seems to have an influence upon the genital system. Furthermore, we have to take into account that the teratomata of the various regions contain different tissue elements (Starling), hence it is possible that teratomata of the pineal gland especially may contain tissue elements which produce substances, and these substances again stimulate to the development of the secondary sexual characters. Among such tissue elements in the teratomata of the pineal gland, we must principally be mindful of the cystic glandular formations, which are often described, formations which, however, seem to originate from the cylindrical ependym of the posterior commissure (organon subcommissurale), rather than from the pineal gland. The opinion that the substances produced by the teratoma itself are the cause of the *pubertas praecox*, of which opinion Askanazy has been the chief proponent, must certainly be taken into consideration in a higher degree than hitherto. But as teratomata must be viewed in the light of formations originating from the exterior, which invade the pineal almost as a sort of parasite, it is unjustifiable to consider them as hypersecreting pinealomata from analogy with the adenomata of the hypophysis which induce acromegaly. Furthermore, it is unjustified to reason from such pathological conditions to the normal function of the pineal gland. Besides, in the development of precocious puberty in the cases of tumors of the cortex of the adrenals, we have an analogy relative to an eventual chemical action originating from these teratomata. As I have pointed out in another place, one cannot, however, reason from that to the function of the adrenal cortex in relation to an action upon the genital development, because these tumors did not probably take their origin from the adrenals as such, but from ectopic portions of the genital anlage (298). The destruction of the pineal gland is another factor which has to be taken into account. But if we consider that this is not the only possible factor, but that, as mentioned, this phenomenon is associated with the presence of an eventually secreting tumor with influence upon the cerebral brain centers and upon certain constitutional conditions, it is unjustified to conclude, as do many others, that it is precisely the destruction of the pineal gland which

causes the *pubertas praecox*. Such a conclusion will be legitimate only when it has been demonstrated, in a series of cases, that an atrophy, without complications, of the pineal gland has induced precocious puberty, in the same manner as in the atrophy of the hypophysis without complications there has been observed dwarfism (*nanism*), which renders probable an influence of the pituitary body upon growth. Nevertheless, in a series of cases of tumors destroying the pineal gland in children, there does not exist *pubertas praecox*; in the same manner as in the above mentioned case of hydrocephalus in destruction of the pineal gland there also did not exist *pubertas praecox*.

We must take into account also the destruction of neighboring brain centers in the mesencephalon. For instance, many authors have expressed the opinion that such destruction is the cause of certain disturbances of development and metabolism in the affections of the pituitary body. But, however, all this question is, at the present day, so unsettled that it is not possible to take a definite standpoint in the problem; we must consider it as a distant possibility, a possibility which has in its favor a somewhat limited probability.

The distant action of the pineal upon the hypophysis can be left out of reckoning, since, in spite of the probable importance of the hypophysis in relation to the sexual functions, *pubertas praecox* has never been observed in association with affections of the hypophysis.

The constitutional element must, to a high degree, be taken into consideration as a possibility. Experience shows that in many cases of diseases in various organs we are confronted by phenomena running a parallel course and of which the one cannot be regarded as the cause of the other. We can mention, as examples, a disease such as tuberous sclerosis in which, coincident with disorganization in the brain, we find formation of tumors in the heart and in the kidneys; another example is the hepato-lenticular degeneration (*Wilson's disease*, *pseudo-sclerosis*), in which the affection of the liver and the degeneration of the lenticular nucleus run a parallel course; or, lastly, a series of cases of pluriglandular insufficiency, in which there exists an action upon quite a number of different endocrine glands.

In the case of complication with tumors of the pineal gland

and pubertas praecox, we must then think of the possibility that we have to do, at the same time, with an anomalous disposition of the region of the pineal gland and of the endocrine elements of the testicles. A case which could indicate a possibility in this direction is that of Goldzieher, where, in addition to the tumor of the pineal gland, existed a hyperplasia of the adrenals, which must be considered as having a relationship to the hypertrichosis. In the case of Raymond and Claude, we find also such an apparent parallelism between the tumors of the pineal gland and a formation of adenoma in the adrenal cortex. Furthermore, we must point out that in nearly all (and possibly all) described cases of tumor in the pineal gland, associated with pubertas praecox, we had to do with teratomata, that is to say, a tumor which has a marked relationship to malformations.

In the cases of teratomata of the pineal gland in which precocious puberty has developed, we have then to take into account the combination of at least three factors: secretion originating from the teratoma, destruction of the pineal gland, and general anomalous disposition of the organism. This does not preclude that the syndrome, pubertas praecox-pineal tumor, presents interest for the diagnosis. But this cannot justify inferences as to the function of the pineal gland, especially as to its significance (inhibiting or accelerating) for the development of the secondary sexual characters.

EXPERIMENTAL INVESTIGATIONS UPON THE PINEAL GLAND

As early as 1898, Howell made the first experiment of injecting extract of pineal gland. However, it was only after Marburg, in 1908, had published his large work on the pineal gland (in which he emphasized its rôle as an endocrine organ) that the experiments were started, partly as extirpation, partly as feeding experiments and injections of the extract. In large part, the experiments gave negative or contradictory results, and, in part, they lacked the necessary experimental control. On the whole, it may be said that there is always a wide field open to experimental research concerning the pineal gland.

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I. Experimental Extirpation

Werner and Boese (1910) destroyed the pineal gland in that it 100 young rabbits. In 6 of them, in which subsequent microscopic examination showed that the destruction had been

total and which had survived a time sufficient to judge the effect, there was not any effect upon the development of genital organs.

In the same year, Sarteschi extirpated the pineal gland in 11 rabbits; 2 of them survived the operation. There appeared retardation in growth and cachexia, which disappeared again. It seemed that the animals remained sterile.

Biedl carried out a large series of experimental extirpations on dogs. Three of them which survived the operation for a period of two months exhibited no symptoms (the three animals were, however, adult). At autopsy it was found that the pineal gland was completely absent.

In 1912, Foà tried total extirpation of the pineal gland in young rabbits, but without any result, because all animals died some days after operation. He was, however, more successful with young chickens, aged 3 to 5 weeks, as 15 of them survived the operation. In the first 2 or 3 months the animals were retarded in their growth as compared with control animals; but afterwards they presented a greater development and, in 3 of them, which were cocks, there appeared a more rapid growth of the testicles and of the secondary sexual characters. Eight to eleven months after the operation there existed a considerable hypertrophy of the testicles and of the combs. The operation was without any effect on the weight of the thymus. With the exception of the retardation of growth during the first months, changes could not be observed in hens; they began to lay eggs at the normal time and the crests did not show hypertrophy. In a series of control animals, corresponding changes could not be ascertained.

In 1912, Christea extirpated the pineal in 30 young cocks; 12 of them survived for a considerable period. The animals which were operated upon presented a marked retardation in development of the genital characters, as comb, spurs, and voice; also the growth of feathers was retarded as compared with that of control animals. The development of the body was not particularly delayed. The animals were rather apathetic. Marked atrophy of the testicles was noted.

Sarteschi published in 1915 a series of new investigations: he performed pineal extirpation on several rabbits and on very young dogs. In the male animals which survived the operation, he found a considerable hypertrophy of the testicles and, in one

of them, he observed, in addition, an important increase in weight and obesity (a thing which Foà did not observe in his chickens). The results in the female animals could not be judged.

Foà, in 1914, also reported new experiments. Of 10 chickens which were operated upon, 7 survived; 5 were hens. The experiments confirmed the earlier results; at first, there was a slight diminution of weight, and afterwards, in the young cocks, appeared hypertrophy of the comb and of the testicles. No corresponding changes supervened in the hens. Microscopic examination of the endocrine glands did not show any abnormality, except changes in the testicles. The canals were wider in the experimental animals. Furthermore, Foà undertook experimental extirpation in 8 young rats, 4 of which survived the operation. On one of these, a female, there did not appear any noteworthy manifestation; in three males, the somatic development attained its maximum more rapidly, but the differences were very soon abolished.

L. Adler, who is right in pointing out that we must expect different symptoms of suppression after pinealectomy in the different animal species, tried, in the year 1914, to destroy by thermocauterization the pineal gland in tadpoles. Out of 350 animals treated in this manner, 100 survived four days. Eight days after, 30 animals were still alive and they were the same size as the controls. After another week, 9 animals were still alive, and in these, during the following period, the development was very irregular by comparison with the control animals. Later on, the majority developed edema, of which they died. There was not any abnormality in the sexual development. The author states that the irregularity of development must be ascribed to the disturbances induced by the pinealectomy in the whole of the endocrine system.

In 1915, Dandy published the results of pinealectomy in dogs. After some negative experiments he developed a technic by which the organ was extirpated from in front, a notch in the posterior portion of the corpus callosum having previously been made. The operation was performed on young puppies, whose ages varied between 10 days and 3 weeks and at the same time on some full-grown dogs. The animals survived the operation for a period averaging from 3 to 15 months. None of the animals operated upon exhibited any change in development or in

psychic condition. Especially, there was not any sexual precocity, nor any abnormality in the sexual organs. The microscopic examination of the endocrine glands did not reveal any change in these. The author concludes that the pineal gland is not necessary for life and does not seem to have any influence upon sexual development.

Horrax (1916) tried, without success, to extirpate the gland in dogs, cats and young rabbits. But extirpation was quite successfully performed in guinea-pigs. Forty-eight of the young animals, in which the operation was successful, lived to sexual maturity or until they were sacrificed. In 15 male animals and in 20 females, the microscopic examination (sections in series) of the brain revealed that the pineal gland has been extirpated *in toto*. The females did not exhibit any difference in the development of genital organs in the operated animals and in the controls. Three of the female guinea-pigs became pregnant, but aborted. The following conditions were found in the male animals: there was not any difference in weight between them and the control animals; but, on the other hand, the testicles showed an average weight of 354 mg. in the operated animals, while they had an average weight of 663 mg. in the control animals. (But it must be said that there were large variations in the total weights and that the author did not make a calculation of the average error.) The vesiculæ seminales were also enlarged and upon the microscopic examination were found more developed. There existed a marked spermatogenesis, but this phenomenon was more limited in the control animals. In rats, in which the extirpation was even more successful, the results were partly brought to nothing by an epidemic. In the few which could be examined, the increase of development in the testicles existed in only one animal; the others presented dubious results.

E. R. Hoskins and M. Hoskins have (1919) removed the pineal gland from 70 young larvae of *Rana sylvatica*, but it regenerated either partially or completely and the larvae grew normally.

If we sum up the evidence on experimental extirpation, the results, as a whole, are seen to be altogether negative. It seems to be established that the pineal gland neither in dogs, rabbits, guinea-pigs nor in hens, is an organ of vital importance. Furthermore, we are obliged to assume that the function of the

organ, in any case, in dogs, rabbits and guinea-pigs, can be taken up by one or more other organs in the case of a suppression. The results which most frequently are considered as decisive are those of Foà. But the results obtained by Christea are totally contradictory to those of Foà. Therefore, it is impossible at the present time, to reach a decision concerning the significance of these experiments.

Concerning Horrax's experiments we must point out that, in spite of their number and technical perfection, the variations in the weight of the testicles were so considerable, as above stated, that one cannot compare the average weights without a calculation of the average error. Yet they show the possibility of an activity of the pineal gland resembling that discovered by Foà in hens.

If we disregard the fact that these experimental results are as yet not confirmed, a question now arises: What part does the pineal gland play in hens, since, although its structure and size are the same as in cocks, experimental extirpation gave negative results? This condition indicates strongly that the action upon the development of puberty, if there really is such, is only of a subordinate and secondary nature.

In comparison with the altogether less valuable injection and feeding experiments, the experimental extirpations are unhappily very few in number, by reason of technical difficulties. It is important that these experiments be extensively repeated. Furthermore, it would be important to undertake such experiments partly on apes and partly on animals which possess a much developed organ, for example, on seals.

II. Transplantation Experiments

Exner and Boese have transplanted the pineal gland with the result that it has soon been completely resorbed.

E. R. Hoskins and M. M. Hoskins (1919) transplanted the anlage of the pineal from larvae of *Rana sylvatica* into 19 other young larvae. It failed to grow.

III. Action of Castration Upon the Pineal Gland

Sarteschi (1910) examined the pineal gland in various castrated rabbits and did not observe any divergences from the normal.

Biach and Hülles (1912) castrated a series of cats, aged 3-4 weeks. Of 15 animals operated upon, 7 males and 2 females survived. Microscopic examination revealed that in the castrated cats the pineal cells were further apart, and the nuclei and the cytoplasm were less abundant; the cytoplasm was darker in color, oftentimes shriveled; the entire cell had lost its rounded form and was angular. The authors think that the cause lies in an atrophic condition of the entire gland as well as the single cells, and they believe that it is the expression of a certain reciprocity. The phenomenon was seen in both male and female animals.

In contradistinction to these results, Ruggeri (1914) found that in rats, after castration, there appeared an increased number of cells and a greater uniformity of the lipoid elements as well as marked development of mitochondria.

Pellegrini (1914) has reported results contradictory to those of Biach and Hülles. (I have not been able to consult his work in original.)

Aschner (1913) examined the pineal gland in pregnant, virgin and castrated guinea-pigs, rabbits, dogs, and cats, respectively. Litter controls were used. In pregnancy, he found the gland shorter, broader and more rounded, while it was more pointed in virgin animals. In the castrated, he observed marked atrophy; that phenomenon was most conspicuous in cats. Histologically, there was in pregnant cats a slight increase of the fat-containing vacuoles which lay imbedded in the interstitial tissue, but these are not specific elements of pregnancy.

The castration experiments as well as the experimental extirpations have thus given contradictory results. We are not entitled to draw from them conclusions concerning the function of the pineal gland and particularly concerning its relationship to the genital organs.

IV. *Electric Stimulation of the Pineal Gland*

De Cyon (1903), in three rabbits, exposed the pineal gland, which he stimulated electrically. Even the slightest contact with the electrode induced slight changes of form in the organ, as it contracted and at the same time modified a little in its position. The author thinks that this should have been ascribed to vasomotor action, if the organ had been very vascular (as is really the case); but, as he did not recognize that, he assumed that the

pineal gland plays a mechanical part in regulating automatically the flow of cerebro-spinal fluid, through the aqueduct of Sylvius. In a way, de Cyon supported his theory by the findings of Nicolas' and Dimitrova's, who observed transversely striated muscular fibres in the pineal gland of oxen. In a later work (1907), de Cyon maintained his opinions. In a like manner, Pellegrini tried electric stimulation (I could not procure the original work). Precisely by reason of the marked vascularity of the organ, no conclusions about a mechanical function can be drawn from the electric stimulation.

V. Chemical Investigations on the Pineal Gland

Fenger collected the pineal glands from a total number of 2358 oxen, 1348 sheep and 5062 lambs. The organs were desiccated in vacuo and a benzine extract was prepared. He determined afterwards moisture, ash, phosphoric acid and total nitrogen. The glands from young animals contained less phosphorus and more total nitrogen than those of full-grown animals.

VI. Injection Experiments

In 1898, Howell injected glycerinated extract of pineal gland. The results were inconstant; in some cases there was no effect, in others the blood pressure was lowered. In any case, the action was different from the constant and characteristic reaction induced by injection of pituitary extract.

De Cyon (1903) injected into rabbits extract of pineal gland from oxen and sheep. He observed that after intravenous administration the heart beats became more frequent and irregular, but there was not any change of blood pressure. Similar, although not quite the same, results are obtained by injection of glycerophosphate of sodium or calcium; he thought, therefore, that the pineal gland influences calcium metabolism. These results seem far from convincing, in consideration of the fact (which de Cyon himself admitted) that the pineal gland often contains calcareous concretions.

Jordan and Eyster have found that intravenous injection of aqueous extract of the pineal gland from sheep produced in rabbits more marked changes of blood pressure than the corresponding extract of other parts of the brain.

Jordan and Eyster found further (1911) that the pineal gland of the sheep contains some substance which, on intra-

venous injection in certain animals, causes a fall of blood pressure associated with a vasodilatation in the intestines, produces a slight degree of improvement in the beat of the isolated cat's heart and causes a transitory diuresis associated with glycosuria in about 80 per cent of the cases. The effect on blood pressure in the cat is small and unimportant. On the whole, the action of pineal gland extracts is relatively slight when compared with that produced by extracts from other glands known to furnish internal secretions.

Dixon and Halliburton repeated the experiments of de Cyon, but found that the injection of extract had no action on heart beat, blood pressure, respiration, intestinal or urinary secretion. Furthermore, they found in later investigations that, while the extract of plexus choroidens and of brain substance injected intravenously in dogs, induced an increase in secretion of the cerebro-spinal fluid, that was not the case with the extract of pineal gland.

Ott and Scott (1910-1911) have made a series of experiments by intravenous injection of pineal extract in lactating goats. The injection had a marked galactagogue effect in the same manner as thymus, corpus luteum and pituitary extract. Preliminary intravenous injection of atropine lessened the galactagogue effect. Further, the injection produced a transitory depression of blood pressure and increase of kidney volume caused by vasodilatation. Also for the male genitalia in cats and probably the mammary gland, the pineal extract acted as a vasodilatator. Application of pineal extract to a uterine strip of a pregnant rabbit caused increased contraction. Local application of pineal extract gave pupillo-dilatation in rabbits when the superior cervical sympathetic ganglion has been excised.

Cushing (1912) obtained negative results on blood pressure and circulation with intravenous injections of the aqueous pineal extract.

Schäfer and Mackenzie (1912) investigated the action of a large number of animal extracts upon the flow of milk from the lactating mammary glands. They were not able to confirm the galactagogue effect of pineal gland extracts reported by Ott and Scott. By later investigations, Mackenzie has found that

intravenous injection of pineal extract of sheep had a slight galactagogue effect, perhaps due to absorption of a small quantity of pituitary extract from the cerebro-spinal fluid.

Dana, Berkeley, Goddard and Cornell found (1913) that by injection of pineal extract in half-grown guinea-pigs, the weight of the animals increased more than the weight of the controls. The same was found in baby guinea-pigs, rabbits and kittens; both weight, size and intelligence were augmented.

Fränkel (1914), by injection of pineal extract, obtained a distinct dilatation of the cephalic vessels and he saw in that action an opposition to the suprarenal glands.

Prior (1915) investigated, in rabbits, aged 10-35 days, the effect of injection of glycerinated extract of pineal gland of calves. Every fifth day, he injected constant quantities. Pure glycerine was injected in the control animals. Weighing and measurement of three animals and of controls showed him, contrary to the findings of Dana and Berkeley, a retardation in growth. No abnormality was found at autopsy. They thought that these results are consonant with those of the experimental extirpations of Foà.

Horrax (1916) injected in the vena saphena externa of extract of pineal gland from calves and from lambs. The application of small quantities did not produce any result. Application of larger quantities there was, after some minutes, a fall in the blood pressure and, corresponding to that, a diminution of the production of cerebro-spinal fluid. The result was the same when the gland was fresh or with desiccated extract.

Ingber (1916) prepared an extract from full-grown oxen and lamb pineals; he studied its action upon the uterus and the results were less marked than was that of the anterior lobe of the hypophysis and much less marked than that of the posterior pituitary lobe. As previous experiments had shown that the effect on pulse rate and blood pressure is also problematic, the author concluded that it is difficult "to consider the pineal body as an internal secretory organ of medical importance."

Bab (1916) found that injection of pineal extract had no remarkable influence on diuresis.

VII. Feeding Experiments

Dana, Berkeley, Goddard and Cornell (1913-1914) have instituted feeding experiments with pineal gland from oxen. Half-adult guinea-pigs, after being fed with pineal gland, showed a more rapid increase in weight than control animals; the same was true of kittens and rabbits. Feeding experiments in children (a boy and a girl) for three weeks gave a little augmentation of the elimination of nitrogen in the urine and, as to the rest, there was not anything noteworthy. Furthermore, they experimentally fed a number of mentally deficient children and thought some improvement in their mentality resulted. Goddard has, however, continued the above mentioned experiments; he found no amelioration after a long period of treatment. Especially, he found that the extracts were quite without effect on certain mongoloid idiots. Later (1920), Berkeley reported that the feeding of kittens, rabbits and guinea-pigs with preparations of pineal gland from calves and young cattle accelerated the somatic growth to a marked degree and that a number of backward children without organic stigmata to whom the gland was administered for a sufficient period made an advance in mental age considerably in excess of any previous progress for a like period.

Dresel (1914) found that pineal feeding (epiglandol) had no influence on the blood sugar.

Hofstätter (1917) treated 11 girls and women suffering from exaggerated sexual libido with pineal medication. In 7 cases he obtained good results. In 3 lactating women he found an augmentation of the milk secretion.

Pilez (1918) treated a case of possible dementia praecox (mania?) with epiglandol and reported some depression of the sexual excitation.

Summing up the results of experimental extirpation and of alimental feeding, we see that they give us in many points contradictory issues and also results. These by nature must be, for instance, amelioration of mentally deficient children after feeding, as these patients may often present spontaneous progress in the course of time. Besides, it is interesting to see how frequently the results of the authors seem to depend upon their preconceived idea either that the pineal gland is an

accelerating organ for development or that it is an inhibiting organ.

Setting aside this part of the question, the action of feeding or of injections of pineal gland extract cannot, in the nature of things, serve to elucidate the function of the organ. We must, for instance, remind ourselves of the fact that the pineal gland is an organ very rich in nuclein and contains, therefore, probably an abundant quantity of nucleinic acid. But in the control experiments it has not been habitually determined whether feeding with corresponding quantities of nucleinic acid induces a similar action on the growth and on the development of the individuals experimented on. Furthermore, we must remember that the pineal gland of oxen and sheep contains an abundant quantity of neuroglia fibers. Feeding with neuroglie tissue from other parts of the central nervous system should thus be considered as a necessary control experiment. All tissues, including the pineal gland, are formed of various substances which are indispensable to the building up of the tissues themselves; but these substances are not an expression of the specific function of the tissues. One ought not to be astonished if many of those substances can produce, by injection or by feeding, alteration of form or function. And as long as these substances are not excluded, most conclusions from experimental feeding or injections must be considered as unjustified.

CONCLUSIONS AND FINAL CONSIDERATIONS

In the present stage of experimental study, our knowledge of the *constitution of the pineal gland* in vertebrates and also in the man has the same extent as our knowledge of the constitution of the other organs of the body.

Our knowledge of the *clinical results of pineal gland tumors* has been enriched, chiefly by the works of Marburg and Frankl-Hochwart, so that we recognize a clinical picture, in which pubertas praecox coincides with teratoma formation in the pineal gland. Thus we may be permitted in a number of brain tumors in children to diagnosticate with a great certainty that the tumor is a teratoma of the pineal gland.

But our knowledge of the *function of the pineal gland* must unhappily be considered as very defective. We can admit of a certainty that this organ has a function in man and in the

majority of mammals. We can further admit as an important possibility that this function is partly an internal secretion, but an internal secretion which is not indispensable to life. Finally, we must confess our total lack of knowledge of the influence of this internal secretion in the body and, particularly, we must point out that the hypothesis that the secretion plays a rôle in the development of puberty is, to date, completely without significant evidence.

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ADDENDUM

The following articles, some of which have appeared after the finishing of my article, are to be added:

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THE PREVENTION OF EXOPHTHALMIC GOITER

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It must be confessed that there is a relative deficiency of interest in the study of the prophylaxis and cure of Graves' disease. Comparatively few medical men can manage to a successful issue a case of this affection, much less an attempt at prophylaxis. That is why operation is resorted to,—not because Graves' disease is medically incurable, but because there are few physicians who make sufficient sacrifices of time and energy to be able to demonstrate perfect non-surgical results. Meanwhile, thyroidectomy is performed upon thousands of these patients, "for better or for worse." If the medical profession were to become half as serious in the prevention and cure of Graves' disease as they are in tuberculosis, not only would many cases of the disease be averted, but surgeons, satisfied that internists can demonstrate excellent results, would refuse to operate on these patients.

A discussion of the prophylaxis of exophthalmic goiter (the rather inappropriate synonym of Graves' disease) does not embrace a consideration of the prophylaxis of simple goiter and of hyperthyroidism. Simple goiter is local, while Graves' disease is a generalized condition. Hyperthyroidism can be produced by the ingestion of thyroid extract; Graves' disease cannot be so produced; and though the syndrome of Graves' disease presents evidences of thyrotoxicemia, there are likewise evidences of dysfunction of the entire chain of endocrine organs and of the vegetative nervous system. Attempts at prophylaxis by the administration of iodine and of thyroid extract are useful in simple goiter; these drugs are not only useless, but hazardous in Graves' disease. Moreover, the use of certain tests to assist in diagnosis of Graves' disease, depending for their usefulness on the flaring up of a dormant syndrome or an aggravation of existing symptoms, cannot be too strongly deprecated as dangerous. The reasons for this are too obvious to be enumerated.

PROBABLE ETIOLOGY OF GRAVES' DISEASE

The study of prevention of any disease must begin with an investigation of its etiology. While in Graves' disease we do not know of any specific cause or causes lending precision to our task, we are cognizant of a series of etiological influences which, if at least partly eradicated, would mean much to the world at large. We know that: (1) hereditary influences play an important part in susceptibility to the disease, as evidenced among other things by the multiplicity of cases in the same family; (2) that this hereditary predisposition may become intensified by acquired factors through errors in the conduct of life or through maladaptation to the world at large; and (3) that in nearly every case of Graves' disease there was superimposed upon predisposition an exciting factor accounting for the onset of the syndrome. We might tabulate the probable etiology of Graves' disease as follows.

A. Inherited predisposing factors.*

1. Autonomic imbalance.
2. Endocrine imbalance.
3. Reduction of threshold of nervous and emotional reaction.
4. Vasomotor ataxia.

B. Acquired predisposing factors.

1. During infancy.
 - (a) Faulty hygiene, diet and discipline.
 - (b) Accidents, as falls, burns, fright, etc.
2. During childhood.
 - (a) As in infancy.
 - (b) Faulty school life; impressions from companions, teachers; overambition.
 - (c) Unhealthy influences of home life; table talk, parental behavior, and other home circumstances.
 - (d) Improper recreation; movies, theaters, reading, etc.
3. During puberty and adolescence.
 - (a) Faulty school life as in childhood.
 - (b) Faulty impressions from home environments, relatives, companions.

*The inherited predisposing factors are interrelated and inseparable.

- (c) Improper recreations: movies, theaters, dancing, reading, etc.
- (d) Inappropriate preparation for adult tasks of life.
- (e) Harmful dietetic and hygienic habits.
- (f) Changes incident to growth and development.
 - i. Physical-thyro-gonadal hyperplasia, menstruation.
 - ii. Instability of mental activity and aberrant assertion of sexual instincts.

4. During adult life.

- (a) Faulty dietary habits.
- (b) Harmful occupational, business, or professional factors; overactivity or inactivity.
- (c) Improper sleep—quality, quantity, and regularity.
- (d) Errors in social and sexual life.
- (e) Faulty mental habits—pessimism, worryment, etc.
- (f) Errors in quality and quantity of recreation.

C. Exciting causes.

1. Physical.

- (a) Focal infections in tonsils, sinuses, teeth, gastrointestinal and genitourinary tracts, etc.
- (b) General or systemic infections, especially tuberculosis, syphilis, and rheumatic fever.
- (c) Autointoxications—intestinal, renal, biliary.
- (d) Neoplasms, especially of pelvis.
- (e) Occupational—extreme physical exertion, hazardous occupations associated with danger to life and limb, exposure to extremes of temperature and to poisons.
- (f) Accidents—railroad, automobile, conflagrations, earthquake, etc.

2. Mental—Psychic trauma (either acute or sustained).

- (a) Occupational—occupations entailing extreme nervous strain, *e. g.*, school teaching, telephone operating; those entailing duties at variance

with the desires of the individual, resulting in continuous distress.

- (b) Economical—maladjustment between income and expenditure, extravagant habits, bankruptcy, etc.
- (c) Social—"high life" and its ambitions; discord with relatives and friends, misplaced love, hatred, jealousy, and other passions.
- (d) Sexual,
 - i. Men—sexual neurasthenia, impotence, priapism, etc.
 - ii. Women—vaginismus, sterility, sexual incompatibility, frequent pregnancies.
- (e) Intense emotional strain—sorrow, anger, chagrin, distress, prolonged engagements.
- (f) Accidents—acute fright, shock, etc., with or without physical injury.

PROPHYLAXIS OF PREDISPOSING FACTORS

What are the precise inherited influences is still uncertain, and to speak of the various theories advanced would entail a duplication of the already voluminous literature. The fact is, however, that subjects of Graves' disease are nearly always spoken of by their parents as having been nervous and delicate during infancy; their childhood was replete with persistent nervousness and semi-emotional outbreaks. There was seldom any complaint regarding progress at school; on the contrary, school work was never a task mentally, though evidently physically fatiguing. Precocity of mind at the expense of physical vitality is frequently described as characterizing school life, though most often these subjects present a floridity of the skin, indicating apparent good health.

So far as I am able to determine in my experience with a large series of subjects of this sort, the earmarks characterizing a young adult possessed of susceptibility to Graves' disease are the following. (1) *Heightened cerebration* is characteristic. Irrespective of the amount of schooling obtained, the ambitions and mental alertness of these persons are beyond those of the average individual of similar station in life. There is frequently a fondness for classical music, a surprising appreciation of the

other aesthetic arts, a desire for psychological pursuits and adventures into the realms of the occult, a craving for literature and lectures apparently beyond the mental reach of the subject; in the professions, an aptitude to reach ahead of contemporaries; in business, ambitions worthy of a captain of industry. It is from this class of individuals that many a talented person or genius arises, if the mental activities are well applied; if not, such a person may become an incipient or an actual case of *dementia praecox*. Occasionally the mental status is somewhat uncertain; conversation upon a topic, though intense and earnest, is unsustained, interest flitting from one subject to another with irrelevant sequence and frequency, bespeaking a veritable frenzy to acquire an encyclopaedia of information within a brief while,—an ambition never satisfied, burning away the energies day after day, to say nothing of the nocturnal activities of the subconscious during attempts at sleep. (2) *Emotional instability* brings about high spirits alternating with moodiness, laughter with tears, and not infrequently intense love with hatred. A happy medium—a stability of feelings and emotions—a degree of the phlegmatic in temperament—these are conspicuously lacking. (3) *Excitable heart and labile pulse* is seen. These subjects are apt to present heart hurry on the slightest physical or mental provocation, with or without palpitation and an “out of breath” feeling. Occasionally, the heart rate is perpetually at a figure somewhat above normal, a characteristic of which the patient is rarely cognizant; but usually the normal rate obtains during repose. The pulse is soft, compressible, and often dicrotic, and frequently indicates a status of sinus arrhythmia. (4) *Vasomotor ataxia* is evidenced by the capillary pulse, dermatographia, the tendency toward hyperidrosis, and sensations of undue heat of the surface of the body, even in cold weather. (5) *The eyes are brilliant or sparkling*, especially during conversation and active attention, when there may be observed at times even a suspicion of exophthalmos. In many instances an imperfect or larval von Graefe’s sign may be elicited. (6) An unusually *palpable thyroid gland* is almost constant in these subjects, though on inspection the thyroid area may appear somewhat full or even normal.

These persons are to be found everywhere—more especially among Caucasians, whose mentality is at the highest state of

development; in all strata of society, rich and poor, male and female, young and old; in all countries; and in almost all climes. While the greatest number may be combed out from the vast multitude of high school and college students, school teachers, stenographers, young business and professional men, real and would-be stock brokers; the young newlywed, the mill hand, the newsboy, and the laborer are not immune. All these are members of a community of mortals who have many things in common, physically and mentally; a generalized instability of the autonomic nervous system and of the chain of endocrine organs; a lowered threshold of emotional and reflex activity; and an ever present danger of the development of an attack of the Basedowian syndrome.

All such persons, especially if presenting a significant history, should be regarded as pre-Graves' disease patients, the object of prophylactic measures. Prophylaxis should consist of endeavors so to plan the individual's attitude and conduct with relation to the world at large as to fortify the bodily forces against Graves' disease. Presented with the opportunity of a free hand in the management of a young person born into a Graves' disease family, what can prophylaxis do to reduce or eradicate this susceptibility? The answer is obviously to avoid or circumvent the acquired predisposing factors above enumerated. The task is a difficult one; guidance must be perpetual, at least up to well established adult life; but if the task is done to within fifty per cent of perfection, the incidence of Graves' disease would probably be reduced by seventy-five per cent of the existing figure.

Acquired predisposing influences are traceable to most of the acts of body and mind of the individual. Born with a standard of physical and mental health at variance with that of his fellows, such a person will not find himself at an equilibrium with those circumstances in life which ordinarily are in entire agreement with the average person. These acquired predisposing factors occur from the very moment of birth and may continue on throughout existence, and unless the maladjustment is corrected through the interference of favorable influences, the persistence of this handicap may mean an attack of Graves' disease.

Every physician knows that an infant is rarely brought up

in an ideal way, *i. e.*, with perfect hygienic, dietetic, and mental management. Nearly always there is a varying degree of error from apparently unimportant trifles to gross carelessness which makes us wonder how the infant can survive the "fond" parents' care. Now, if one or both parents happen to be susceptible to, suffering with, or recovering from Graves' disease, we have in the offspring an instance in which hygienic, dietetic, and mental care *must* approach the ideal. To permit the baby to "just grow" is to invite a strong predisposition or inflammability to Graves' disease. For safety's sake, such children should be regarded as pre-Graves' disease subjects and, as such, the object of prophylaxis from the very beginning. The most important suggestion to parents should be the matter of not accustoming the child to flesh food. Parents are apt to consider flesh food as necessary to the attainment of growth and strength, and may begin administering steaks, chops, and the like at the early age of twelve or eighteen months. This is the first gross and most important error that could be committed.

When school life is begun, other factors become operative. Mental impressions from teachers, classmates, companions, relatives, and even parents may diminish or increase susceptibility to the disease, depending upon whether they approach or recede from the ideal. The quality and frequency of indulgence in recreation, whether at home, out of doors, or in assemblies at theaters, halls, and the like, play their part with a potentiality that is not sufficiently appreciated. The "movies" are a most powerful factor in molding the mental health and character of young America.

During puberty and adolescence, added recreational factors arise, in that the contact with the opposite sex tends to increase the existing emotionalism and mental disquietude almost, and at times, to the point of irrationality. In this category may be mentioned parlor games, inappropriate stage performances, and dance halls. An attempt must be made tactfully to avert these errors. Overambition in school and college duties and in the preparation of a career should likewise be under control. Females with a predisposition to Graves' disease must obtain complete physical and mental repose during the menstrual period, since menstruation is interrelated with the neuro-endocrine system, which latter is in a state of varying degree of

excitability at this time. Irritability, hot flushes, weakness, emotionalism, outbursts of hysteria and temper are commonly seen prior to and during menstruation. Also, at this time, a distinct temporary hyperplasia of the thyroid gland with unmistakable though mild evidences of Graves' disease, may assert themselves. In girls and young women engaged in active pursuits, this bit of advice may be difficult to follow; but when regarded in the light of serious future events, a mutual understanding on this subject is usually reached without much ado.

It is during early adult life that the greatest peril exists in persons predisposed to Graves' disease, in that faulty dietary, social, sexual, vocational and other factors may intensify susceptibility to the utmost. Dietary and related habits which tend toward an increased intake of toxins (and here the habit of constipation may be included), place a great strain upon the detoxicating mechanisms of which the endocrine organs, especially the thyroid, are a part. These patients are often passionately fond of meats, frequently taking large quantities more than once daily. This habit may be discouraged by an intimate conversation with the subject, with an explanation of the why and wherefore. I am frequently told by patients suffering with the disease that unless they take three, four or more cups of coffee daily, they are at loss to know what to do. The personal history indicates that the patient has been a slave to coffee and tea for years. Here, too, an explanation to the effect that coffee and related beverages are partially the cause of the illness and inimical to a favorable progress toward health, usually results in satisfactory cooperation, and the error is eradicated. The same, in essence, may be stated of the various spices, condiments, and other harmful substances of food and drink.

One of the most difficult problems facing the internist is the prohibition of the use of tobacco in persons addicted to the use of the weed for many years. Extra-systole and the various cardiac arrhythmias and even auricular fibrillation are more commonly seen in tobacco users of this class of individuals than in others. Unless the habit is stopped at once, all other efforts to assist our subject will prove fruitless. It is my custom to have the patient promise faithfully at the first visit never to touch tobacco again. I do not permit them to say "I'll try" or "I'll do my best," much less do I permit a gradual weaning away

from the weed. Anything less than "I shall" implies effort with a minimum of determination and is a poor psychological procedure; "I shall" is usually successful; the patient stops using tobacco, and that is all there is to it. I frequently explain that a part of the tobacco habit consists in giving the muscles of the mouth something to do; the taking of chocolate coated nuts, chocolate peppermints, or crackers, when the craving for tobacco arises, will accomplish the same purpose, and these substances being nutritious, will at the same time improve weight and increase strength.

Though a goodly percentage of predisposed individuals possess normal weight and a few are to a degree obese, most are undernourished. These subjects require an avoirdupois to correspond at least to their height and age. Indeed, a ten per cent increase in weight above the person's standard is highly desirable. The surplus serves as a safety point representing an amount of reserve to be relied upon in case of emergency stress and strain. These subjects are commonly poor eaters, though the appetite may be good or excessive. Many have sharp hunger several times a day, but it is quickly satisfied, unsustained and capricious. Thus in response to hunger, the intake of food is equivalent to one-half the customary meal, and this, repeated throughout the three meals per day, corresponds to a smaller daily intake than that of the average individual. Even an occasional "bite" between meals does not yield the number of caloric units required by a person of similar age and stature. The patient has accustomed the stomach to hold comfortably just so much and no more at a sitting, as a result of which the taking of a normal quantity of food causes discomfort. Correction should aim at persistent endeavor to accustom the organ to take at least a normal quantity of nourishment daily, irrespective of discomfort and other apparently undesirable consequences. In the course of several weeks of forced feeding, the subject finds himself eating plentifully, the weight reaches normal and soon above normal, and the ten per cent excess, our goal, is attained. A proper stomach capacity is now permanently fixed; the weight is indicative of a more normal resistance to physical and mental emergencies.

The question of occupation is frequently a serious one. Aside from possible physical deterioration resulting from the

pursuit of certain occupations associated with undue physical exertion, poisoning by lead, phosphorus, arsenic, mercury, and various noxious gases and impurities, there are occupations in which mental strain is a vital factor. Telephone operating with its nerve-racking incidents, school teaching, with its well known potentialities for restless working hours and quite as restless hours off duty as a consequence, social work among the poor and suffering, with its depression—these pursuits, though in the abstract the choice of the persons whose lives are devoted to the work, still carry with them very deteriorating influences upon body and mind. And if we take into account the numerous instances in which the occupation of an individual, such as manual labor, salesmanship, stenography, housekeeping,* and divers other pursuits are forced upon the person in question, and far from being a pleasure, are a perpetual drudge and torture to life, especially in the cases in which there is too little leisure and too much work, we can readily see how important is an investigation of the influence of the daily duties of the person under our study. We must not ignore the occasional unfortunate case of the man or woman of leisure who has become overly introspective for lack of something else to do. Lastly, there are a few occupations which, though not a drudge to the person in question, are associated with the *possibility* of acute mental or emotional strain, which possibility may serve as a sword of Damocles. Among these may be mentioned employment on the topmost floor of a tall building, with its possibilities of fire or elevator accidents, employment in locations where explosions are possible, as in or near chemical laboratories and munitions plants, and others of like nature. Our task must entail an attempt at elimination, or at least reduction of occupational faults which interfere with the maintenance of an equilibrium between internal bodily conditions and external circumstances.

An ominous subjective symptom in this class of individuals is persistently unrefreshing sleep with or without disturbing dreams. A person of this sort frequently arises in the morning feeling not refreshed, rested, and ready for the day's work, but

*The housewife often presents a problem entirely her own. Especially is this true in the presence of children and the absence of a servant. The manifold routine duties of kitchen work, looking after the children, house cleaning and the like, with almost no outdoor air and social existence, deteriorate physical and mental health and serve as a potent predisposing factor in the production of Graves' disease.

fatigued, weary, and anxious to remain in bed, irrespective of the hour and caring little for breakfast. Such a status, occurring daily and prolonged for months or years, is a strong predisposing factor in the development of Graves' disease, and should be overcome by sane, persistent remedial measures calculated to induce healthful, refreshing sleep for at least eight out of twenty-four hours. It may be discovered that nine and even ten hours of sound sleep daily are required in order to secure the necessary physical and mental well-being. In this respect every person is a law unto himself, and the peculiarities of each subject must be investigated and evaluated without any hard and fast adherence to conventional standards. In general, the patient with a known predisposition to Graves' disease should be encouraged to devote an *extra* hour or two each night to sleep or relaxation, for the purpose of reinforcing the autonomic and endocrine stability against possible disturbing influences through the waking hours.

The strenuous life of the times—the mad rush to earn the dollar and the equally mad tear to spend it—coupled with the tendency in some quarters to illicit affections and its implications—all these and allied factors cannot be ignored in the consideration of causal relationship and the prophylaxis of Graves' disease.

Were a careful sexual history obtained as a routine procedure, very valuable information would be elicited, facts which are otherwise missed to the detriment of the patient. Often we find that the sexual perturbation of puberty and adolescence, and indeed the thyroid hyperplasia are continued indefinitely on into adult life. In both sexes, the sexual and emotional restlessness should be tempered by appropriate social, emotional, and aesthetic influences. The status of being affianced, marriage, and pregnancy, in addition to the general sexual thoughts of the individual, are subjects which cannot be overestimated in this respect; it is here, perhaps, more than elsewhere in the consideration of the prophylaxis of Graves' disease in the adult female that common sense and vigilance should be exercised.

Faulty mental habits are almost the rule in these subjects. Aside from those already implied, temperament or disposition must be so influenced as to approximate the ideally consistent as closely as possible. Many possess an undue hypersensitiveness; they are "thin skinned" and often pessimistic. Though high

colored in attitude when things are to their liking, trivial difficulties and obstacles may turn tables so completely that moodiness, gloom, tears, and even hysteria prevail. To change this vascillating mental make-up into one of dependable stability, permeated by a healthy quality and quantity of optimism, though a difficult task, can at least in part be accomplished through the subtle influence of tactful friends or relatives, or under the guidance of a capable mentor. How to increase the threshold of emotional reaction is the vital problem. The substitution for a state of emotional alertness or *qui vive* by an attitude of *sang froid*; in other words, the assumption of the so-called "phlegmatic" temperament by one to whom every mole hill is a mountain, is the "consummation devoutly to be wish'd."

Though the prevention or reduction of the predisposing influences of Graves' disease may appear an abstruse affair, vague in its deductions and in many instances difficult of conception, much can be done by an inculcation into the individual of principles which, in course of time, would diminish discord and increase equilibrium between inherent peculiarities and susceptibilities on the one hand and controllable habits and environments on the other. The adherence to the broad principles of the *simple life** and the discovery and fortification of weak links or vulnerable points in the subject's make-up, with an eye to individualization, will finally bring about the desired equilibrium in sufficient degree to be highly gratifying to all concerned. Having attempted the achievement of this objective, the next consideration is the avoidance, as far as is in our power, of the known exciting factors.

PREVENTION OF EXCITING FACTORS

If in most persons with a susceptibility to Graves' disease we can prevent the occurrence of an exciting factor, the chances are highly in favor, not only of the enjoyment of relatively good health, but also of unusual longevity. In the absence of an attack of the disease, these persons, for some unaccountable reason, are known to exceed the span of three score and ten, and occasionally approach and even reach the century point.

The exciting factors are far more tangible and traced with

*The best place for a subject of this type to reside is away from the seashore; preferably in the country and at moderate altitude, if possible;—a place where the simple life most likely characterizes existence.

less difficulty than the predisposing causes. Given a subject of the type above described, place him in an automobile going at the rate of 40 miles an hour, and rush the machine across railroad tracks just in time to avert a collision with an approaching train, and the mechanism of Graves' disease is begun. There need not be an accident. Psychic trauma, with or without physical injury, is the most usual history obtainable as the starting point of Graves' disease. Following an earthquake, or a fire in a large factory in which many are employed, a massacre, the wreck of a liner in midocean, experience on the firing line in battle, or in other situations of imminent danger to life, forty-nine out of fifty persons soon recover physical and mental poise and are themselves again. One of them, however, because of the singular susceptibility, may evince no psychic and endocrine recoil or adjustment to the previous neuro-endocrine balance. The trembling, the staring eyes, the cold, clammy skin, the heart hurry, and other features expressing fright, remain, become chronic or "frozen," and we are confronted with a case of Graves' disease. The torch of an exciting cause in the form of the acute emotional strain or psychic trauma, applied to the inflammable subject, means a beginning of the syndrome of the disease. Earthquakes, lightning storms, tidal waves, and other natural phenomena which engender many cases of Graves' disease, are beyond human effort to control. War conditions, conflagrations, explosions, elevator accidents, shipwrecks, massacres, automobile and train accidents, and other conceivable situations associated with danger to life and limb are man-made and therefore at least partially avoidable. Unfortunately, these conditions are not in the power of doctors or psychologists materially to control, and therefore not substantially amenable to their prophylactic efforts. It is reasonable to assume, however, that even if exciting causes cannot be averted, if we succeed in reducing in a given subject the degree of susceptibility to the affection, the onset of Graves' disease may be prevented.

Certain circumstances characterized by less acute but more sustained emotional strain and which ordinarily serve as predisposing factors, are likewise exciting causes. Especially is this true if the predisposing errors in question become intensified, and if the susceptibility of the individual is unduly great. It is from this class of subjects, the small minority, that we fail to

elicit a history of psychic trauma or acute emotional strain as the starting point of the syndrome. Extreme illness or the death of a loved one, emotion such as hate, anger, jealousy, and the prolonged strain of such occupations as school teaching, telephone operating, and the like, unrequited love and sexual maladjustments may serve both as predisposing and exciting causes. With regard to the latter, it must be emphasized that sexual neurasthenia, priapism, and impotence in men, and in women prolonged engagements, sexual incompatibility, vaginismus, sterility, multiple pregnancies, and allied conditions, are potent exciting causes and largely amenable to prophylaxis, depending upon the tact and skill of the medical attendant.

Focal infections, though regarded by many as the most important of exciting causes of Graves' disease, are in my experience more often coincidental than causal in the majority of instances. Though I firmly believe that focal infections should receive proper attention, whether in tonsils, teeth, nasal sinuses, gastro-intestinal or genitourinary tract, the percentage of patients actually cured by tonsillectomy, removal of teeth, gall bladder, appendix, colon, and other parts of the body found to be at fault, is remarkably small. That a causal relationship has been assigned to a mere coincidence is obviously the case in many patients. It must be insisted upon, however, that irrespective of their etiological importance, focal infections require prompt attention.

Frequently tuberculosis and syphilis, and occasionally acute rheumatic fever, are provocative of the syndrome of Graves' disease, and require expert management. The same may be said of autointoxication, whether it be renal, biliary, or intestinal.

Neoplasms, especially fibroids of the uterus and adnexia, are at times exciting factors of Graves' disease. I have observed a few instances of startling amelioration of the syndrome following the removal of a uterine fibroid. But in a discussion of the relationship of a nonhyperplastic thyroid growth, a note of caution must be sounded, lest erroneous etiological theories of Graves' syndrome be entertained. A thyroid adenoma, in course of time, may give rise to hyperthyroidism, and thus we are confronted with the so-called toxic adenoma. This is not synonymous with Graves' disease, and the removal of the adenoma cures the patient. On the other hand, Graves' disease is not due to hyper-

thyroidism, but to a generalized dysfunction of the autonomic nervous system and of the entire endocrine chain; hence thyroidectomy is disappointing in the therapeutics of the affection.

The prophylaxis of Graves' disease must also include a consideration of the prevention of relapse after recovery from an actual attack. In all patients in whom complete recovery has been firmly established and maintained for a year or longer, we may safely assume that the predisposition to the disease has at least been materially minimized, if not altogether eliminated. This is especially true of patients in whom thyroidectomy was not depended upon, but who were fortunate enough to have been under the care of an experienced internist, with resulting approach to the normal or arbitrary standard of bodily and psychic health and the usual resistance to Graves' disease. Such a person, having recovered from this dread affection, has been habituated during treatment to obedience to the required principles of hygienic, dietetic, and mental daily life. Taught how to eat, how to work, how to sleep, and even how to think, this individual is living practically an "anti-Graves' disease" existence, and has become more useful than ever to self and society.

CONCLUSIONS

1. Prophylaxis of Graves' disease by individual and organized effort is timely and important. The devotion of more time and energy by internists and general practitioners to the study of the diagnosis, prophylaxis and treatment of this affection would not only reduce the number of sufferers, but would in course of time place the therapeutics of Graves' disease on a strictly nonsurgical basis.

2. Ideal prophylaxis of Graves' disease should begin in infancy and extend well into adult life, the object being an attempt at perfection in hygienic, dietetic and mental discipline.

3. During childhood, such additional influences as school and home life, companions, recreation, and other factors capable of molding the physical and mental self must be taken into account.

4. During the restlessness of puberty and adolescence, the emotionalism, instability of reasoning processes, and the physiological thyro-gonadal hyperplasia, all make for an accentuation of neuro-endocrine instability, and should receive most thoughtful, scrupulous guidance.

5. In general, an individual standard of conduct to self and the outside world must be formulated for these individuals. It is a two-fold task—each contributing equally to the achievement of the goal, viz.: (a) the adjustment or adaptation of the circumstances of life to the singular peculiarities of the individual, and (b) the modification and adaptation of the peculiarities of the individual to the circumstances of life.

6. Predisposition to Graves' disease is not always markedly amenable to prophylaxis, nor are exciting causes of the disease always avoidable. In the absence of the ideal (the *eradication* of predisposing and exciting causes), if we can *reduce* susceptibility on the one hand, or *modify* the *chances* of the occurrence of exciting factors on the other, the prophylaxis of Graves' disease will have earned an important place in preventative *medicine*.

7. The question involved is not that of a "lump on the neck." We must firmly understand that a subject of Graves' disease is no more a victim of goiter than is a sufferer with typhoid fever one of splenomegaly. The elimination of this disease from the classification of goiter is the first real step toward a better understanding of the etiology, prophylaxis and treatment of this, the most interesting affection in the domain of *medicine*.

HYPERTHYROIDISM: A NEW CLINICAL SIGN

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It has no doubt occurred in the practice of many clinicians that in a short period of time several cases of the same type have appeared for examination. Krehl called this the "Duplicitate die Felle."

In the course of the physical examination of patients, a group presented themselves with a certain objective finding, the exact clinical significance of which was not appreciated until it recurred again and again, and finally registered the impression that its occurrence was something more than an accidental symptom of no especial value.

Just behind and below the sterno-clavicular junction, about 1 to 2 cm. either to the right or left, is the anatomical position of the inferior thyroid artery. Over this area a bruit is heard which is unlike the murmur over the gland when it is visually or palpably enlarged. In fact it may be present when both of these factors are absent. This sound is *hissing* or siren-like in character as differentiated from the *whirring* or water-wheel churning sound heard over the gland itself. The hissing character of the sound over the artery is the point I would emphasize as new and distinctive of hyperthyroidism, or of potential hyperthyroidism. The sound is heard more frequently on the right than on the left side, but in marked cases when there is considerable evidence of thyreotoxicosis it is present on both sides. It is not transmitted to any of the other blood vessels of the neck or superficial vessels of the trunk or extremities, and I have never heard it over the superior thyroid vessels. It is increased by deep inspiration, and is not lost during expiration. It is systolic in time and is lost during the rest period in the cardiac cycle. Accompanying the hissing bruit, but with no definite degree of constancy, is a palpable thrill in the cubital artery.

In all, it was present in 12 cases, 2 men and 10 women. Without going into the detailed history of these cases, which is

immaterial for our purpose of discussion, the exciting causes which led to the hyperfunction of the thyroid may be classified as follows: Brain work or mental strain, puberty, tuberculosis, pregnancy, excessive intercourse and toxic conditions, *i. e.*, septic tonsils.

This observation extends over a period of about one year, during which time as a matter of routine all patients were examined to determine whether or not this sign occurred in conditions other than hyperthyroidism, and included a number of normals. Especial care was exercised in the examination of high blood pressure cases, particularly those of 200 or over, and one case of over 300 in which I was unable to measure the pressure because of lack of markings on the instrument. No evidence of the bruit was found in any of them. I was unable to produce the hissing bruit by pressure or manipulation of the bell of the stethoscope on any of the arteries, in any cases other than those in which the subjective symptoms checked with the objective signs and justified the diagnosis of hyperthyroidism.

The diagnosis of hyperthyroidism was checked by basal metabolic determinations and the estimation of the sugar tolerance. In some cases the rate was normal, in others it was increased. The sugar curve showed an analogous variation from normal to retention with the presence of sugar in the urine. These findings are consistent, however, with available clinical data, as there are cases of toxic goiter reported in the literature with a normal basal metabolic rate.

Another striking characteristic of the bruit is its evanescence. It is not constant, but is apparently dependent upon the heart action for its production. In those cases in which the heart action is accelerated and there is a precordial thrill, the bruit is present, as is also the cubital thrill. With the general amelioration of the symptoms, due to rest or the administration of iodine, these signs disappear. This clinical fact is not at all at variance with certain experimental work, and with clinical observation carried out on a large series of cases. It would appear, then, that its production is dependent, first, upon an accelerated and increased heart action, and, secondly, upon a consequent increase in the rate of the blood stream. The possibility of a third condition, namely, arterial changes having an influence, will be discussed later.

Plummer (1) has shown that "if a patient, having a colloid goiter with bruit, thrill and palpable thyroid arteries, is given 5 to 10 mg. of thyroxin intravenously, or a corresponding dose of desiccated thyroid by mouth, the bruit will diminish in from three to six hours, the thrill and palpability of the arteries will disappear in from twenty-four to thirty-six hours. This reaction takes place in all cases." The bruit referred to in the literature is the one heard over the gland itself, as I find no reference or description of the hissing bruit over the blood vessels in any of the writings on the clinical evidence of hyperthyroidism.

The circulation in hyperthyroidism has always presented an interesting problem to the clinician. While the preponderance of study on thyroid disease has been done by the pathologist on the gland itself, there still remains to be explained certain constitutional manifestations and symptoms which pathologists do not clarify. The clinician is reluctantly forced into the field of theory in order to explain them. It has been said that "in the analysis of most clinical as well as didactic problems, much that is not definitely known must be bridged over by theory." If, then, we build our theoretical bridge and prop it by our clinical experiences, looking to the pathologist for reinforcement, we may be able to build a structure that will stand the weight of further investigation.

The pounding, heaving pulsations of all of the superficial blood vessels in thyroid hyperfunction, coupled with a palpable increase in the thickness of the vessels and a rise of blood pressure, lead to the thought that besides the local effect on the thyroid itself, an increase of circulating thyroxin must exert a constitutional effect upon the arterial system which is more or less lasting.

In the terminal branches of the arterioles where the muscle tissue predominates, there is opportunity for great expansion and strong contraction. Since this mechanism is under the control of the sympathetic system, which is also involved in hyperthyroidism, it is not too much to assume, from a clinical standpoint, at least, that this vasomotor instability produces an increase in the muscle coat of the systemic arterioles, with a concomitant influence on blood pressure. This influence exerted on the heart brings about left-sided hypertrophy, increased blood pressure, albuminuria and other symptoms found in hyperthyroidism,

which are referable to arteriosclerotic changes. Let us see for the moment if this theory finds substantiation in the pathological studies on the gland.

Crile (2) has mentioned the fact that in many cases of goiter the superior and inferior thyroid arteries are considerably increased in size so that a distinct pulsation can be felt throughout the entire gland.

Wilson (3), whose description of the pathology of the vascular changes within the gland in exophthalmic goiter is the most exhaustive I have found in the literature, is of the opinion that the gland is hyperemic, and that this condition is demonstrable both grossly and histologically; further, that this increase in vascularity is not due alone to an increase in the size of a few large arteries and veins, but also to a diffuse general increase in the size of the small arterioles and capillaries.

Kendall (4) states that "the immediate effect of an intravenous injection of thyroxin causes no change in blood pressure, pulse rate, nervous manifestations or other hyperthyroid symptoms; but the long continued presence in the tissues of the body produces the picture of hyperthyroidism, ending in great emaciation and death." It was, therefore, demonstrated that the long continued presence of thyroxin caused death from secondary reactions and not from its direct toxicity.

Sistrunk (5) is of the opinion that while some patients improve under medical treatment, it is unwise to allow it to continue over too long a period of time because they are apt to have marked degenerative changes in their vital organs.

If we assume the toxic origin of the changes in the blood vessels to be true, we may ask ourselves two pertinent questions.

1. *Is there an analogous condition of the blood vessels found in which similar murmurs are heard?*

I recently examined a case of arterio-venous aneurysm, in which I was impressed with the similarity of the murmurs. In this patient the hissing murmur was present in practically all of the blood vessels, not only in the thigh, but also in the femorals, illiac and thyroid vessels; in fact, all of the superficial blood vessels. The case was parallel to the one reported by Osler (6), in which a patient with circooid aneurysm developed multiple aneurysms following typhoid fever.

A case in point was reported by Fernell in the St. Louis

"*Courier of Medicine*" in 1887. "A man, aged twenty years, had a large pulsating tumor above the clavicle, which had lasted many years and which involved all of the branches of the thyroid axis, except the inferior thyroid. During an attack of measles the temperature rose to 106.5 and the tumor looked red and angry and pulsated very strongly as if about to rupture. Following the attack of measles the tumor began to subside gradually, the thrill disappeared and it shrank to a mass of hard connective tissue which could be rolled about. It has further been shown that no structures retain their powers of growth in greater degree than the arteries. Many physiological conditions demand the retention of this property; for example, the arteries of the uterus at term are four or five times as large as in the unimpregnated state."

These examples of the capability of the arteries to change in caliber and lose certain apparent pathological conditions by a peculiar and innate power of size regulation which is essentially their own, serves in a striking manner to illustrate the point with regard to the presence and absence of the hissing sound as controlled by the improvement of the patient on the one hand, and the toxic origin of the changes on the other.

2. Can the murmur be produced by reaching the physiological limit of thyroid medication in hypothyroidism?

I have seen two such cases, one in a child six years of age and the other in an adult.

Following the administration of desiccated thyroid extract for a period of two months the child grew two inches and gained six pounds. It then developed a tachycardia, was nervous, and on listening over the inferior thyroid, the hissing bruit was heard. The gland was not palpably enlarged. The adult case presented practically the same result, except for the fact that the symptoms of hyperthyroidism were much more pronounced. There was extreme nervousness, insomnia, sweating and distressing tachycardia. This experience demonstrates that with the physiological development of the hyperthyroid state, the hissing murmur develops as a part of the clinical syndrome.

In the back swing of the pendulum from its long upward flight, accelerated by the enthusiasm placed on the value of the increase of the basal metabolic rate as a pathognomonic expression of hyperthyroidism, and the failure of the constancy of the

glucose tolerance test, the clinician again finds himself struggling with the same problems of diagnosis which he met before the laboratory was called upon to aid in the interpretation of clinical problems. The more one sees of negative laboratory findings the greater should be the impression upon the mind of the diagnostician that more thought, time and energy must be given to the upbuilding of objective clinical signs, which are independent of the laboratory and through the development of which the value of thorough physical examinations will be greatly enhanced.

The pathologist should not be expected, even by a careful study of the tissues, to give a true interpretation of the clinical symptoms of a given disease and, vice versa, the clinician should not be looked to for a pathological diagnosis. It is in such misdirected attempts that errors in clinical diagnosis are inevitable. The fitting together, however, of these two elements will hasten the day of the ideal in medicine, and will elevate the art of diagnosis to the pedestal from which it has been so ignominiously removed.

From these studies I have come to the following conclusions:

1. The hissing murmur in the inferior thyroid artery is associated with toxic hyperthyroidism.
2. There are pathological changes found, for the most part in the systemic arteries, due to circulating thyroxin when present for an extended period of time.

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EXOPHTHALMIC GOITER FOLLOWING VARICELLA AND MASTOIDITIS IN A CHILD WITH STATUS THYMOLYMPHATICUS

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The Polyclinic

SEATTLE, WASHINGTON

Buford (1), who has recently reviewed the incidence of Graves' disease in young children, states: "I have reviewed both American and foreign literature carefully for the last twenty years and find eighteen cases reported in children under twelve years of age. I find only two cases in which operation has been performed. My patient (third to be operated) was six years old, the youngest one that has been reported as operated." Nine cases, including the one reported by Buford, have been reported in children under five years of age. Another case is herewith presented.

REPORT OF CASE

Case No. C. 966; 5-26-1922; C.C., female, age 4 years and 7 months.

Family History: The father is somewhat nervous, has high blood pressure and a rapid pulse; his eyes are moderately prominent, but apparently normal. The mother's eyes are also prominent. The paternal grandmother died of heart trouble; the maternal grandmother died at child birth; the grandfather died of tuberculosis of the kidney; the aunt has throat trouble; the uncle is living and well.

Chief Complaints: Nervousness, exophthalmos of both eyes, frequent urination, loss of weight and rapid pulse are the most prominent symptoms.

Clinical History: The child's birth was normal. She was very sickly during the first six months. She was weaned early. More or less stomach trouble has been manifest since birth. She has always been high strung, very active, and mentally bright and alert. She had more or less trouble with the glands of the neck. She was talking at 12 months; lisping was noticed early. She sat alone at 8 months, crept at nine months, walked at 18 months, and laughed aloud at 4 months. She got her first tooth at 7 months, and had a full set at 2 years. She had influenza and tonsillitis in 1920. The tonsils and adenoids were removed in 1920. She had chicken-pox early in 1922. She complained of mastoiditis, April, 1922.

The present conditions developed following chicken-pox in April, 1922, and continued up to the time she consulted me. An operation for the relief of the mastoid condition had not been deemed advisable by her otologist. The eyes, although normally large, rapidly gained prominence following the attack of chicken-pox. The patient weighed

Age	Measurements			
	Weight (Pounds)	Height (Inches)	Chest Cir. (Inches)	Head Cir. (Inches)
Birth	7.75	21.50	14.00	15.75
6 months.....	13.50	26.00	16.50	17.50
12 "	21.00	29.50	17.50	19.00
18 "	25.00	32.50	20.00	20.00
24 "	28.00	34.75	20.50	20.50
36 "	32.00	38.00	21.50	20.50
55 "	36.00	44.50

40 pounds prior to the onset of mastoiditis, lost 10 pounds during the active stage of her trouble and weighed 36 pounds at the time of examination. Along with the development of eye symptoms there appeared tachycardia, gastrointestinal irritability as evidenced by attacks of vomiting and a tendency to diarrhea, and an overwhelming lassitude in spite of her extreme restlessness and emotional excitability. She complained at times of pains in the back, hips and arms. The pulse ranged from 110 in the early morning to 140 at night. There was frequent desire to urinate; sphincter control was normal. Sleep was not sound nor restful. Vomiting attacks occurred frequently—"on the slightest provocation." These attacks were associated with yellowing of the skin and marked dehydration. There was marked nocturnal diaphoresis at times.

Physical Findings: The patient is 44½ inches in height, 36 pounds in weight and is poorly nourished. Her skin is moist and of fine texture. Her blood pressure is 90/45; pulse, 148 lying down; buccal temperature, 99°F. She has an abundant head of hair, dark, of fine texture, and with moderately low anterior attachment. The



Fig. 1. Photographs showing the degree of exophthalmos and the small degree of enlargement of the neck due to hyperplasia of the thyroid.

eyebrows and lashes are well formed; hair is absent on the remainder of the body. The eyes markedly protrude. The sclera show above the cornea when the patient looks straight ahead; there is marked widening of the palpebral fissures (Dalrymple and Stellwag's sign), and weakness of convergence without diplopia (Mobius' sign); involuntary blinking is infrequent (v. Stellwag's sign); other eye symptoms are hippus, large pupils, dryness of the eyes, inability of the upper eyelids to follow the descent of the eyeball (v. Graefe's sign), fullness of both upper and lower lids, pale conjunctivae, no tremor of the lids nor nystagmus of the orbs. The lids can be forcibly closed over the cornea; pressure on the orbit slightly accentuates the pulse; pupillary reflexes to light and distance are lively.

The ears are large and set at a wide angle to the head. There is tenderness over the mastoids. The cervical and inguinal glands are

palpable; the tonsillar fossae are empty; because of adenoids breathing is through the mouth. The teeth are in fair condition, small and pearly white. The palatal arch is high; the speech is lisping; the voice is high pitched and rather harsh; there is a tendency to drool; there is a dry, unproductive cough.

The neck is full, showing anterior and lateral enlargement of moderate degree; there are marked pulsations; the goiterous mass is soft.

The heart rate is rapid—145 to 148 when lying down; there is no arrhythmia; a musical systolic murmur is heard best at the base of the heart, transmitted to the upper left chest and neck; a distinct thrill is discernible over the left infraclavicular region; the area of cardiac dullness is increased in all diameters. Mediastinal dullness is marked, wider than the sternum.

Breathing is shallow and rapid, 25 to 40 per minute; sighing is frequent; respiration is of the abdominal type; breath sounds are rough; there are no rales. The patient is pigeon breasted and has a prominent abdomen. She would not permit palpation of the epigastric region.

Reflexes are very active, but otherwise normal. The rectum, genitals, spine and joints are negative. Muscular development is poor; fat deposits, light. Coordinated movements are executed gracefully. There is slight gross tremor of the extended hands, but no Rombergism. She is continually fidgeting and talking, is of a friendly, good-natured disposition, and is keenly interested in her surroundings. A mental test made by Dr. Stevenson Smith, who referred the case to me, showed the physical and mental ages to be equal, *i. e.*, normal mental development for her age.

Laboratory Findings: The urine has a specific gravity of 1022, is alkaline and contains no sugar, albumin nor casts; phosphates are abundant. The blood is made up of: hemaglobin, 80 per cent; erythrocytes, 3,600,000; and leucocytes, 6,800; the differential count shows neutrophils 36; small mononeuclear 59; large 5. Dr. K. J. Holtz reports the results of a radiographic examination as follows: "Heart shadow enlarged; unable to differentiate aortic shadow from others in the mediastinum. Mediastinal shadow approximately 3 inches wide, regular in outline, continues from the heart shadow upward into the neck. Inflammatory areas in the region of the hili, particularly on right side; probably glandular. Epiphyses of wrist and hand open."

DIAGNOSIS

The case was diagnosed as exophthalmic goiter and status thymolympathicus.

TREATMENT AND PROGRESS

Because of the size of the thymus gland and the known risk of operative procedures in patients with status lymphaticus it was deemed best first to attempt reduction of the gland by radiation and later to ligate the thyroid arteries or remove a part of the thyroid gland, depending upon her progress.

On May 31, 1922, the pulse was 144; blood pressure, 88/35 to 50; temperature, 98.8°F. On June 2, the patient received 84 millicampere minutes' radiation over the thymus area (distance 16 inches, gap 8¼ inches, 4 mm. aluminum filter). During the

afternoon the child ate ice cream. She vomited several times that night. Nausea and vomiting continued until June 5. During that period the pulse varied between 124 and 148. The temperature remained normal. June 30, the patient spent a week in bed following her arrival home, suffering from a "bilious attack." During that attack her skin did not turn yellow as upon previous occasions of a similar nature. The urine at this time, as upon June 5, showed numerous granular casts, considerable albumin and a great amount of solid material including urates. Her sleep had been greatly disturbed since radiation. The appetite was variable; the stomach, extremely irritable; there was diarrhea with mucus in the stools; and short sighing respiration.

July 1, a radiogram showed marked decrease in the diameter of the substernal shadow. Hili shadows were prominent with considerable lateral radiation. The patient received a second x-ray treatment over the thyroid area of the same strength as the first. Within a few hours following the treatment nausea and vomiting set in and continued until July 5. On July 3, the evening temperature was 100.5°F.; pulse, 150; respiration, 40. On July 4, the temperature was 99°F.; pulse, 150; respiration, 40. The urine showed but a few casts and pus cells, considerable albumin, and much solid material. July 8, the pulse was 104; there was no elevation of temperature; the urine was greatly improved. After this the patient returned home and passed from observation.

DISCUSSION

It appears that my patient showed signs of lymphatism soon after birth. This condition was evidenced by the enlargement of follicles at the base of the tongue and pharyngeal lymphatic growths in the nose. The enlargement of the tonsils led to their early removal and, as usual for this type of case, "she has never been right since."

It is likely that the attack of influenza during the same year as the removal of the tonsils and adenoids aggravated her condition; however, it was not until after an attack of chicken-pox that the thyroid disturbance became manifest. Two months following the onset of chicken-pox she contracted mastoiditis. This infection greatly and rapidly accentuated the thyroid symptoms.

*Similar results followed removal of the tonsils in a young girl seen by me in St. Louis, in whom a large thymus gland was found and successfully treated by the use of the x-ray.

The series of infections, it seems, might be considered as a causative agent in the production of the hyperplastic goiter. This assumption is in accord with the findings of McCarrison *et al.* To quote Janney (2), page 800:

"The hyperplasia of thyrotoxicosis is best explained, just as in other thyroid hypertrophies, as an attempt at compensatory regeneration to make up for cellular exhaustion and injury due to toxic or other causes. We have thus an acceptable explanation for the thyroid hyperplasia of Graves' disease arising from local or focal infections, intestinal toxemia and bacterial infections—hyperplasias not susceptible of reasonable explanation by the hyperthyroid theory."

Adler (3), in 1917, contended that diseases of the thymus are able to produce Graves' disease with or without disease of the thyroid. He concludes that his experiments prove that Graves' disease never is due to an abnormal function of the thyroid, but that the goiter is caused by Graves' disease. In Graves' disease, according to Klose (4), the thymus is next to the thyroid in importance in that it undergoes morphological changes—"epithelization." The two glands can cause a general hyperplasia of the lymphoid system. Simpson (5) calls attention to the frequency with which exophthalmic goiter is associated with enlargement of the thymus, and advises that x-ray therapy precede operative measures on the thyroid. According to Janney (2), page 806:

"A diffuse adenohyperplasia is regularly found in Graves' disease (Kocher, F. v. Müller). This may include the tonsils, spleen, and intestinal follicles. The lymphoid cell infiltration of the thyroid itself is best considered an expression of the same general process. It is probable that the thymic enlargement, in spite of efforts to bring out a more specific relationship, is but an instance of the general *status thymolymphaticus* present (Capelle; Eddy). The lymphocytosis and mononucleosis present in both hypothyroidism and exophthalmic goiter are probably due to this *status lymphaticus*."

Melchoir (6) points to the fact that the thymus is large in from 75 to 85 per cent of patients suffering from Graves' disease. Nordmann (7) believes it necessary in every operation for Graves' disease to look for the thymus. In patients with symptoms of *status lymphaticus* or hypoplasia of the sex organs the

thymus should be removed before attempting operative measures on the thyroid. Haberer (8) also is of the opinion that thymus destruction should constitute a part of the treatment of patients suffering from an enlarged thymus and Graves' disease.

From a review of the literature it is concluded that the proper management of patients suffering from Graves' disease and status thymicus is destruction of the thymus gland by the use of radiation and the surgical removal of part of the thyroid gland. Such a line of treatment was planned for the present case; however, because of withdrawal of the patient, this could not be carried out.*

Thymic destruction because of radiation was evidenced in my patient by the marked decrease in the size of the organ as shown radiographically and by the appearance of a great amount of solids in the urine. Further, it appears probable that the rapid destruction of the gland and the consequent demand made upon the excretory organs was the causative agent in the production of the transient nephritis following x-ray therapy. This assumption is more convincing when it is recalled that the urine was negative as to albumin and casts before such treatments, although the patient was convalescing from an attack of mastoiditis.

The blood picture in the present case appears to be that of lymphatism; however, as is well known, a lymphocytosis is characteristic of exophthalmic goiter [see quotations from Janney (2)]. The leucopenia perhaps gives at least an associative explanation for the frequency of, and low resistance to, infections. It therefore appears that the reduction in the number of polymorphonuclear cells, even at a time of mastoiditis (a condition usually not associated with leucopenia), was one of the predisposing factors to the repeated infections which finally resulted in the production of a toxic goiter.

CONCLUSION

Consideration of the present case suggests a definite relationship between infectious processes and the development of a

*The patient underwent an operation for partial thyroidectomy by her local physician soon after her last x-ray treatment. The pulse, according to her mother, ranged between 94 and 140 after the operation. The weight increased to 52.5 pounds. Her rest, appetite and general condition became greatly improved. There was cessation of vomiting and increased bowel activity. She lost weight during a recent attack of grippé.

On April 4, 1923, an examination showed the pulse to be 102, standing. Her weight was 47.5 pounds and her height 47.25 inches—a gain of 2.75 inches in 10 months. The exophthalmos was somewhat reduced. There was but a slight coarse tremor of the extended hands.

THE SEX COMPLEX. W. Blair Bell, London. 1920. Bailliere, Tindall & Cox. 2 ed. 251 p.

The issue of a second edition of this book within four years indicates that, though treating a rather special subject, it has been highly appreciated. The style of the book is very readable, though oversimplified and more or less superficial and incomplete. It deals with secondary and primary sex characteristics and with the interrelations of the different endocrine organs. The last hundred pages are devoted to the pathological and psychical disorders of the incertory organs as related to sexual characteristics.—J. K.

Abstract Department

(ADRENAL)—Hirsutism in a boy of 12. Basal metabolism study (Hirsutisme chez un garçon de douze ans. Étude du métabolisme basal). Apert (E.), Stevenin & Broca (R.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1750-1753.

Typical case of hirsutism, the patient having the basal metabolism of an adult man.—F. S. H.

Paroxysmal severe adynamia in amyloidosis of the ADRENAL cortex (Paroxysmale schwerste Adynamie bei Amyloidose der Nebennierenrinde). Bauer (J.), Klin. Wchnschr. (Berl.), 1922, 1, 1595-1597.

A man of 66 years complained of oppressed respiration after the least physical exercise. Every day he had 2 to 3 sudden attacks, even being unable to raise his head at times. He died during one of these attacks.—J. K.

Growth of the cortical and medullary substance of the ADRENAL gland and their volumetric relation. Histological-biometric research on *Cavia cobaya* (Accrescimento delle sostanze corticale e midollare della glandola surrenale e loro rapporti volumetrici. Ricerche istologiche-biometriche in *Cavia cobaya*). Castaldi (L.), Arch. di fisiol. (Florence), 1922, 20, 33-127.

From measurements of 34 male, and 37 female guinea pigs, and numerous fetuses, and a comparison of these observations with previous results, the author concludes as follows: The inter-renal body is visible in the 7 mm. embryo as an outgrowth of the coelomic epithelium. The immigration of the medullary element has not begun in the 18 mm. fetus, but in that of 32 mm. it is distributed through the inter-renal body, occupying about one-fourth of the whole volume, but not yet giving the chromophil reaction. Subsequently, while the medulla is drawing together to the centre, it diminishes relatively, and at birth is about one-fifth the size of the cortex. In only two cases was the medulla found much dispersed at birth. The actual weight and volume of the male adrenal is greater than that of the female of like age in both prenatal and post-natal life. The volume, relative to body weight, is greater in the female, even in utero. The left gland is usually larger than the right. The adrenal grows continuously, and increases relatively to body weight. The cortex shows parallel growth, more regularly

in the male; that of the female shows a sudden increase in the second month (puberty). The medulla, compared with total body-weight, shows relatively little increase, with marked oscillation, and diminution during periods of greatest cortex growth, and in old age. In advanced age there is marked absolute and relative cortex increase. The medulla has greater specific gravity than the cortex. It averages one-ninth the volume of the cortex. The ratio is a function of age and diminishes from birth. In the gravid female the cortex hypertrophies; during lactation it returns to normal. In only one animal, a female, was a cortical body visible macroscopically. All the data fall into line with physiological, pathological and clinical data emphasizing the importance of the adrenal, and especially of the cortex, in connection with body-growth. The original paper must be consulted for actual figures.—A. T. C.

Observations on the relation of the ADRENAL glands to the blood pressure response during cerebral anaemia in cats and rabbits. Coombs (Helen) & Rogoff (J. M.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1922, 20, 41-43.

In cerebral anemia repeated short occlusions of the head arteries may result in a change of the typical curve of blood pressure usually produced by cerebral anemia. There are two distinct parts to this modified curve. Winkin has suggested that some product of adrenal activity is responsible for the second part of the rise. The authors have tested this by using cats and rabbits in which the adrenals were tied off or excised. The absence of all secretion does not modify the curve. The number of blood pressure responses to cerebral anemia that can be produced is dependent largely on the general blood pressure in the animal at the time the arteries are occluded.—J. C. D.

Malignant hypernephroma of the right ADRENAL (Malignes Hypernephrom der rechten Nebenniere). Fraenkel (E.), *Deutsche med. Wchnschr.* (Berl.), 1922, 48, 1370.

Case report of a girl of 9 with a beard, much hair on the trunk, a great deal on the pubes and a very large clitoris. Postmortem examination showed that there was hypernephroma of the right adrenal, with hyperplasia of the left. In the large ovaries scarcely any follicles were found.—J. K.

(ADRENALS) Paroxysmal tachycardia and melanoderma of Addison type. Sympathicotonic pathogenesis (Tachycardie paroxystique et mélanodermie du type Addisonien. Leur pathogénie sympathicotonique). Gilbert (A.) & Coury (A.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, 46, 1596-1609.

Studies in fatigue. XII. The effect of ADRENAL secretion on non-fatigued and fatigued skeletal muscle. Gruber (C. M.), *Am. J. Physiol.* (Balt.), 1922, 62, 438-441.

"Adrenal secretion evoked by splanchnic stimulation increases the height of muscular contraction of both the non-fatigued and fatigued skeletal muscle." It therefore cannot be regarded as a specific antagonist to the so-called fatigue substances.—T. C. B.

The ADRENALS and anaphylaxis (*Surrénales et anaphylaxie*).

Képinow (L.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 327-329.

Having studied the rôle of the thyroid in anaphylaxis, the adrenals have been studied in the same manner. The removal of the major part of the suprarenals does not prevent shock when sensitizing injection is made after the operation; on the contrary, guinea pigs show a much greater sensibility to the intoxicating dose than do the normal controls. This increased sensibility does not manifest itself in passive anaphylaxis.—T. C. B.

Influence of various conditions on the ADRENAL vessels. Masuda

(T.), *Acta scholae med. univ. imp. (Kioto)*, 1922, **5**, 57-74; abst., *Physiol. Abst.*, 1922, **1**, 506.

Adrenaline (1 to 10,000-50,000) constricts, and lower concentrations have no effect when perfused through the adrenals.—R. G. H.

ADRENAL tumor (*Tumor der Nebenniere*). Melchior, *Klin.*

Wchnschr. (Berl.), 1922, **1**, 2115.

ADRENALS and PANCREAS antagonism (*Sull' antagonismo fra*

surrenali e pancreas). Moscato (G.), *Folia med. (Napoli)*, 1922, **8**, 353-366.

The adrenals of normal dogs 3 or 4 kg. in weight contain about 1 mg. of adrenalin. After ablation of the pancreas and succeeding experimental diabetes there is an increase in the size of the adrenals, which contain as much as 4 mg. of adrenalin; this is lost in 14-24 days after the operation. Thus it is shown that at first decreased pancreatic function causes increased adrenal function, but that later, due to lack of stimulation from the pancreatic hormone, the adrenals function less than normal.—G. C.

(ADRENALS) Addison's disease and pigmentary cirrhosis (*Maladie*

d'Addison et cirrhose pigmentaire). Oddo (C.) & Oddo (J.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, **46**, 1578-1581.

(ADRENALS) On the experimental basis of the theory of gangraena

arteriitica SUPERENALIS. Oppel (V. A.), *Lancet (Lond.)*, 1922, **ii**, 116-121.

The following criticisms of the theory of the cause of spontaneous gangrene have been given in a previous communication. In the coagulation of the blood certain protein-forming amines are

formed possessing vasoconstricting powers and therefore the vasoconstricting effects of the serum may be ascribed, not to adrenaline, but to amines. In the blood plasma from such cases it has never been possible to prove that the vaso-constricting substance was adrenaline. Adrenaline is a substance that breaks up so rapidly that it is not found in the peripheral vessels. Oppel answers these criticisms as follows. The blood serum of spontaneous gangrene cases is richer in vaso-constricting substances than normal serum; whether it is due to adrenaline or not has not been shown. The degree of dilution of the plasma—500 times—used in the laboratory investigations and the degree of sensitiveness of the analyzing apparatus are the causes of the negative results. The separated ear of the rabbit and the separated human finger are not sufficiently sensitive to physiological quantities of adrenaline because of the initial spasm of the arterial walls. In the separated fingers 1 in 50,000,000 solution of adrenaline produced no vasoconstrictor effect. Very approximate estimates of adrenalin in the blood are dilutions of 1:3,000,000,000 to 1:15,000,000,000. Further the isolated ear of the rabbit is complicated by oedema of the tissues, which also obscures the reaction. As to the duration of adrenaline in the circulating blood, the shortest period for its breaking up is 30 seconds, which is about half the circulation time, hence it can not fail to reach the peripheral vessels. In some personal experiments on rabbits, the femoral or axillary artery was tied and 1 or 2 cc. of 1 in 10,000,000 or 20,000,000 solution of adrenaline in Locke's solution was injected into the distal end of the artery. When the rabbit was freed there was a delay in the movements of the foot with contractures of the extensor group of muscles. With the stronger solutions there was complete paralysis of the wrist which wore off in about 3 hours. Controls with ligation and injection of Locke's solution gave no such reaction. It is estimated that the dilution of adrenaline in the peripheral vessel after mixing with the blood is 1 in 40,000,000 to 80,000,000. This indicates that living tissue reacts more energetically to adrenaline than separated ears or

R. E. K.

diagnosis of Addison's disease (Le diagnostic de la maladie d'Addison) Sézary (A.), Bull. et mém. Soc. méd. d. hôp. 1922, 1572-1575.

made that any asthenia which is not accompanied by rapid muscular weakness is not of adrenal origin.

Studies in the pathogenesis of Addison's disease (Le diagnostic de la maladie d'Addison) Sergent (E.), Bull. et mém. Soc. méd. d. hôp. 1922, 1679.

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The supposed relation of the ADRENALS to reflex volume changes in the denervated limb. Stewart (G. N.) & Rogoff (J. M.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 20, 36-37.

When the central end of a peripheral nerve is stimulated the volume of the hind limb, previously denervated by section of the anterior crural and sciatic nerves, increases coincidently with the rise in blood pressure, and then diminishes to less than the initial volume. Bayless explains this as a reaction of the muscular coat of the arteries to stretching. Von Anrep claims that it is due to increased output of adrenin. The authors get the reaction in dogs after the adrenals have been removed. While not excluding adrenin as a factor, they conclude it is not a necessary one for this reaction and that Bayless' explanation is satisfactory.—J. C. D.

Histopathology of the ADRENAL capsules in various nervous and mental diseases. (Contribution à l'histopathologie des capsules surrénales dans les diverses maladies nerveuses et psychiques). Vasilescu (C.), *Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy*, 1922, 3, 41-44 (January).

Lipoids are found in large amounts in the adrenal cortex in cases of senile dementia, nephritis, tuberculosis, meningitis, mongolism, melancholia, and general paralysis. A little less is present in cases of epilepsy, dementia precox, and pellagra. The glomerular zone seems particularly well supplied in manic depressive psychosis and hydrocephalus. Sclerous tissue is found in pellagra; general paralysis, melancholia and senile dementia. Adenomas were found in manic-depressive psychosis, mongolism and general paralysis. Cortical hyperplasia was found in dementia precox, epilepsy, general paralysis and hydrocephalus. The medullary substance was very much reduced in the cases of melancholia.—F. S. H.

(GONADS) Relation of the female sex glands to the ADRENALS and THYMUS (Über Beziehungen der weiblichen Keimdrüsen zu Nebennieren und Thymus). Walter (H.), *Frankfurt Ztschr. f. Path. (Weisb.)*, 1922, 27, 276-289.

The paper consists of an analysis of the autopsy findings in 61 females varying in age from a few days to 83 years. In comparing the body weight and length with the weights of the suprarenals, ovaries and thymus the author found that old age and chronic cachectic diseases induced ovarian atrophy but has no notable influence on the weight of the suprarenals. He observed that in sexually mature individuals with persistent thymus the ovaries were quite large even when the suprarenals were not hypoplastic. No parallelism between the fat content of the ovaries and the suprarenals was noted.—H. L. J. (D. M.)

The ADRENALS and cortical epilepsy (Surrénales et épilepsie corticale). Wertheimer (E.) & Dubois (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 301-303.

H. Fischer asserts that following ablation of the suprarenals in rabbits convulsive substances (amyl nitrite) and cortical excitation, even by strong currents, no longer cause convulsions. The observations were repeated on dogs, as rabbits are known to be refractory to cortical epilepsy. After suprarenal ablation in dogs, cortical excitation is followed by the same tonic and clonic spasms of the muscles, with the other symptoms accompanying epilepsy of this type in intact animals. Experiments are described, and the tone of the article is critical.—T. C. B.

The beginning of function in the SUPRARENAL medulla of pig embryos. Weymann (M. F.), *Anat. Record (Phila.)*, 1922, **24**, 299-313.

The chromaffin reaction first appears in embryos having a length of 40 mm. At first it is faint and does not occur in all cells of the medulla. By 75 mm. all such cells show the reaction.—W. J. A.

The influence of d-, l-, and dl-ADRENALINE on beating and not-beating heart-strips [Das Verhalten des Herzstreifenpräparates (nach Loewe) unter verschiedenen Bedingungen. II. Versuche über den Einfluss von l-, d-, und dl-Adrenalin auf den schlagenden und nichtschlagenden Herzstreifen]. Abderhalden (E.) & Gellhorn (E.), *Arch. f. d. ges. Physiol. (Berl.)*, 1922, **196**, 608-628.

The limiting concentrations producing action on the beating heart-strip of the frog are: l-adrenaline 1:15 million, dl-adrenaline 1:7.5 million, d-adrenaline 1:1.5 million. At the limiting or slightly higher concentrations the action is very transitory, but lasts longer with increased concentration; the duration of action is less with d- than with l-adrenaline. In high concentrations both produce, besides the increase of contraction, a slowing. Higher concentrations are required to stimulate the automaticity of a not-beating than of a beating strip.—A. T. C.

A comparison of the atheromatous action of organic and synthetic ADRENIN (Action athéromatogène comparée des adrénalines organiques et synthétiques). Arloing & Thévenot, XVI Congr. franç. de méd. (Par.), 1922, Oct. 12-14; abst., *Presse méd. (Par.)*, 1922, **30**, 926.

After the injection in rabbits of 12 drops, given in 5 doses over a period of 24 days, or of 10 drops, given in 4 doses over a period of 28 days, the authors found that synthetic, levogyric adrenin, more hypertensive than racemic adrenin, caused more atheroma, and also

that it was twice as atheromatogenous as organic adrenin. They conclude, therefore, that the atheromatous effects are not in direct relation with the hypertensive, vasomotor effects, since two adrenins, having identical action on the vasoconstrictors, differ so profoundly in their toxic effects on the aorta of the rabbit.—R. G. H.

Glandular physiology. LIV. Leon Asher. Demonstration of ADRENALIN in arterial blood (Beiträge zum Nachweis von Adrenalin in arteriellen Blut der Tiere). Asher (L.) & Schneider (C.), Biochem. Ztschr. (Berl.), 1922, 133, 373-390.

Rabbits were used in these experiments. The superior cervical ganglion of one side was extirpated. The injection of strychnine into the otherwise uninjured animal produced marked pupillary dilation on the side of the operation and only minor similar reaction on the normal side. After the splanchnic nerves had been extirpated on both sides, the pupillary reaction to strychnine could not be produced. The latter phenomenon is attributed to a lack of increased adrenalin secretion following the strychnine stimulation of the splanchnics, and as a proof of the presence of adrenalin in the major circulation under normal conditions.—F. S. H.

Death by ADRENALIN in the course of chloroform anesthesia.

Cardiac syncope (De la mort par l'adrénaline au cour de l'anesthésie chloroformique. Synope cardiaque). Bardier (E.) & Stillmunkes (A.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 321-324.

The death of chloroformed animals following injection of about 0.01 mg. of adrenalin per kg. body weight is the result of cardiac syncope accompanied by fibrillation, as established by Levy in 1911. It consists in intoxication of the myocardium. It resembles the ordinary chloroform syncope, but its mechanism appears to be different.—T. C. B.

Calcium salts and ADRENALIN in the treatment of fractures (Sali di calcio ed adrenalina nella cura delle fratture). Battaglia (M.), Rassegna Internaz. di clin. e terap. (Napoli), 1922, 3, 459-460 (October).

The author has obtained good result in the treatment of fractures—whether open or closed—by adding to the usual treatment adrenalin 10 drops 1:1000 and 10 cgm. calcium phosphate twice a day. The treatment proved efficacious in the formation of normal callous as well as in offsetting the effects of nervous traumatism. The author attempts no explanation except to advance the theory that adrenalin mobilizes the calcium salts in the organism.—J. V.

Thermo-electric studies of temperature variations in animal tissues.

III. ADRENALIN. Crile (G. W.) & Rowland (Amy F.), Am. J. Physiol. (Balt.), 1922, 62, 370-382.

By means of a specially devised thermo-couple, temperature changes in the brain and other organs under various conditions were observed. The response of the brain to injections of adrenalin was so uniform as to justify a separate report. The temperature of the brain and thyroid was increased by adrenalin. The liver and voluntary muscles were not affected. In the absence of the liver adrenalin produced no change or a diminished temperature. There was no reaction after thyroidectomy. Under ether the reaction of the brain was greater than in normal animals; under nitrous oxide, less. Many charts are included.—T. C. B.

The blood picture after injection of ADRENIN in blood diseases (*Das Adrenalinblutbild bei Erkrankungen der hämopoetischen Organe*). Hittmair (A.), *Ztschr. f. klin. Med. (Berl.)*, 1922, 95, 366-383.

Changes after injection of adrenin are not typical and do not enable diagnosis of special changes in the function of organs or tissues of the body. The injection of 1 mg. may be followed by the occurrence of pathological blood cells in the blood stream, but this cannot be considered as proof of an increased formation of blood cells. They are found only when they are previously on the point of coming into the blood.—J. K.

The rôle of ADRENALIN in the hypertension produced by exciting the splanchnic nerve (*Nouvelles expériences sur le rôle de l'adrénaline dans l'hypertension produite en excitant le nerf splanchnique*). Houssay (B. A.) & Marconi (A. P.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1049-1052.

To answer the objection of Stewart and Rogoff, the circulation in dogs was reduced to the head, thorax, anterior extremities, suprarenals and one posterior foot by suitable ligatures. Under these conditions stimulation of the splanchnic causes an elevation of pressure and at the same time the denervated hind foot diminishes in volume. If the lumbo-capsular vein is occluded, no such change occurs. The authors conclude that excitation of the splanchnic causes an adrenal discharge.—T. C. B.

The rôle of acid in ADRENALIN hyperglycemia (*Ueber die Rolle der Säurewirkung beim Zustande kommende Adrenalinhyperglykämie*). Kornfeld (F.) & Elias (H.), *Biochem. Ztschr. (Berl.)*, 1922, 132, 192-211.

Subcutaneous injections of adrenalin in rabbits induce hypocapnia of some hours duration. This phenomenon is not produced in dogs. When man is similarly treated there occurs either no reaction or, more frequently, a minor lowering of the CO₂ tension of the alveolar air and it is of short duration. Hypocapnia, therefore, is not an essential preliminary for adrenalin hyperglycemia.

The question as to whether a local acidification of the liver is of significance in adrenalin hyperglycemia was not answered by these studies.—F. S. H.

Studies of Graves' syndrome and the involuntary nervous system.

IV. The vascular response of the pithed cat to single intravenous injections of ADRENALIN. V. The vascular responses of the pithed cat to repeated intravenous injections of equal doses of ADRENALIN. VI. Attempts to alter the vascular response of the pithed cat to repeated injections of similar doses of ADRENALIN. VII. On the mechanism of sensitization to subcutaneous injections of ADRENALIN. Lieb (C. C.) & Hyman (H. T.), *Am. J. Physiol. (Balt.)*, 1922, 63, 60-93.

Papers I and II of this series will appear in *Am. J. M. Sc.*, paper III in the *Arch. Int. Med.* early in 1923. Papers VIII and IX have appeared in the *J. Am. M. Ass.*, 1922, 79, 1099; 1213. In the present papers the vascular response of the pithed cat to adrenalin has been taken as a satisfactory index of the functional state of the myoneural junctions of the involuntary nervous system. Pithing was considered incomplete if the blood pressure was higher than 50 mm. hg. or if it varied spontaneously 15 per cent. The response to a single intravenous injection is analyzed and its latent period, ascending and descending limbs and fastigium are discussed. In fatigue the reaction is of longer duration and the return to normal delayed, showing that sensitiveness to adrenalin accompanies atony rather than tonicity of the thoracico-lumbar division. In the vascular response to repeated injections there is a constant variable when all known variables are controlled. It consists of a progressively increasing response and has been called "sensitization"; it is necessary to eliminate this "sensitization" before factors that alter adrenalin response can be given their true value. Before a substance can decrease adrenalin response it must overcome the sensitization effects; of all substances tried, Mg. alone showed a specific diminution of response. Sensitization is probably due to an alteration in the peripheral structures of the involuntary nervous system. The first subcutaneous injection of adrenalin has no effect, but succeeding injections may give a clear-cut sensitizing reaction. The mechanism is probably the same as for intravenous injections and as in the latter is independent of the thyroid. There is no scientific basis for the value of the Goetsch test.—T. C. B.

The influence of ADRENALIN on metabolism in various excised tissues. Martin (E. G.) & Armitstead (R. B.), *Am. J. Physiol. (Balt.)*, 1922, 62, 488-495.

The addition of adrenalin to the solution results in an augmentation of the production of CO₂ in frog's muscle. In the present paper, it is shown that this is not specific. Frog's brain, mesone-

phros, liver, stomach tissue and intestinal tissue, all show a two- or three-fold augmentation of acid production in the presence of adrenalin.—T. C. B.

ADRENALIN in weak heart action (*Insufficiencia cardiaca e adrenalina*). Moreira (da F. J.), Arch. brasil. de med. (Rio de Jan.), 1921, 11, 1-10.

As regards the neurogenic or myogenic origin of asystole a great deal of importance must be accorded to hormone insufficiency (adrenalin, hypophysis). The author has obtained amelioration of symptoms in severe asystole by the injection of 0.5 mg. of adrenalin.

—B. A. H.

The passage of ADRENALIN from the cerebrospinal fluid into the general circulation (*Le passage de l'adrénaline du liquide céphalo-rachidien dans la circulation générale*). Nitzescu (I. I.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 818-820.

Results of the passage of adrenalin from the cerebrospinal fluid into the general circulation, usually determined by its effect on blood pressure, have been divergent. The author observed the changes in blood sugar and in the leucocyte picture. Dogs were injected without anesthesia into the subarachnoid space, traversing the atlanto-occipital membrane, and fluid was withdrawn equal to the amount of solution injected. Such injections were followed by an increase of blood sugar, and leucocytosis, and it was concluded that adrenalin passed into the circulation from the cerebrospinal fluid, but its passage was so slow that it had no appreciable effect on blood pressure.—T. C. B.

— **(ADRENALIN) Vasodilator mechanisms. III. The action of nicotine.** Ranson (S. W.) & Wightman (W. D.), Am. J. Physiol. (Balt.), 1922, 62, 405-415.

Of endocrine interest in that after nicotine has paralyzed the dilator mechanism adrenalin still produces its characteristic vascular changes.—T. C. B.

— **Comparative pressor power of racemic and laevo ADRENALINE.** Richaud (A.), J. de pharm. et chim. (Par.), 1922, 26, 81-86.

Racemic adrenaline employed in small doses of the order of 0.01 mg. increases the blood pressure to a somewhat less degree than laevo adrenaline, but the difference is not great, but varies from 10 to 15% in general, although it may be as much as 25 to 30%. As the dose is increased to 0.04 to 0.05 mg. the difference in activity disappears, and as the usual therapeutic dose is 0.04 to 0.1 mg. there is no disadvantage attendant on the use of the racemic compound.—Physiol. Abst., 7, 448.

(ADRENIN) Barium-epinephrin antagonism on the excised surviving intestine. Roth (G. B.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 43.

This antagonism, previously reported by the author in frog's intestine, can likewise be demonstrated with strips of intestine from the rabbit and turtle.—J. C. D.

The technic of ADRENALIN studies in man (Zur Methodik der Adrenalinuntersuchungen am Menschen). Rothmann (M.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 936-937.

The author discusses the reasons for different authors observing different effects from the injection of adrenaline. To obtain uniform results three conditions are necessary. The subject must be in such a state of mind that the adrenalin has no influence on psychical functions (in man injection of scopolamin-morphin generally secures this). Adrenalin must be injected intravenously; this is quite harmless when such amounts as 0.1 mg. are slowly injected. The blood pressure must be measured with an exact instrument. The apparatus of Riva-Rocci, which is ordinarily used for this kind of work, is not exact enough. If these precautions are taken the first effect of an injection is decreased pulse rate with a rise of blood pressure. An increased pulse rate shows that psychical processes have changed the effect of adrenalin.—J. K.

Further experiments on ADRENALIN (Weitere Untersuchungen über Adrenalin). Stuber, Ruszman & Proebsting, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1568.

See Endocrin., 6, 671.

Melanins of ADRENIN origin (Melanine di origine adrenalinica), (Ueber Melanine, die aus Adrenalin hervorgehen). Saccardi (P.), Arch. di fisiol. (Florence), 1922, 20, 205-208; also Biochem. Ztschr. (Berl.), 1922, 132, 439-442.

Concentrated chlorine-water was added to 300 grams of official adrenaline-hydrochloride (Givandan and Laverotte). From this solution, changing to rose-red, then yellow, a colloidal brown solution was obtained after 24 hours, from which, when acidified with hydrochloric acid and evaporated on the water-bath, black flecks (0.25 gram) separated. (The Parke-Davis preparation gave no colloidal solution but a black precipitate after 24 hours.) The amorphous black substance was soluble in water, and two-thirds soluble in 95% alcohol, the soluble portion giving reactions similar to the natural melanins and the "pyrrol-black" of Angeli.—A. T. C.

(ADRENIN) Lactic acid formation after sugar puncture (Zur Frage der Milchsäurebildung nach Zuckerstich). Sammartino (V.), Biochem. Ztschr. (Berl.), 1922, 132, 215-217.

Piqûre of rabbits is followed by an increase in the lactic acid content of the liver, but not to so great an extent as that following adrenalin administration.—F. S. H.

Action of ADRENALIN on the change during alimentation and fasting (*Azione dell'adrenalina sul ricambio durante l'alimentazione e nel digiuno*). Susanna (V.), *Folia med. (Napoli)*, 1922, 8, 234-244.

Dogs were experimented on. The results were doubtful, but in general it appeared that elimination of nitrogen and of the salts diminished during alimentation when adrenalin was administered. The contrary was due during fasting.—G. C.

Physiological ADRENALINEMIA (*Existe-t-il une adrénalémie physiologique?*). Tournade (A.), *J. de méd. et de chirurg. de l'Afrique du Nord*, 1922.

If cross-circulation is made between the suprarenal vein of one dog and the jugular of a second, then after stimulation of the splanchnic in the first all the adrenaline effects (raising of blood pressure, etc.) result. Doubt thrown on the theory of hypo- and hyper-glycemia by the negative results obtained by simple injection of blood from a stimulated dog is thus not justified.

—*Physiol. Abst.*, 7, 447.

Intravenous infusion of normosal and ADRENIN in collapse caused by peritonitis or after operations (*Die intravenöse Dauertropfinfusion mit Normosal und Adrenalin zur Behandlung des peritonischen und postoperativen Collapses*). Wiedkopf (O.) & Hilgenberg (F. C.), *Beitr. z. klin. Chir. (Tübing.)*, 1922, 127, 229-237.

The authors recommend in collapse continuous intravenous infusions of normosal (a kind of Ringer's solution) containing 1 cc. 1% adrenin per L. Forty to 60 drops should enter per minute. In very severe cases the first half liter is given quickly. Two and a half to 4 liters are given daily. Quick improvement of the pulse rate is the first symptom of success. Prognosis is best when micturition remains normal.—J. K.

(ADRENIN) Effects of transfusion of carotid blood taken during splanchnic excitation (*Effets de la transfusion de sang carotidien recueilli pendant l'excitation du splanchnique*). Zunz (E.) & Govaerts (P.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 881-882.

The authors tried to show the presence of adrenalin in the blood after stimulation of the splanchnics, by a crossed transfusion in dogs. Their results were negative.—T. C. B.

(AUTONOMIC NERV. SYST.) Pathology of the sympathetic. Brown (W. L.), *Encéphale (Par.)*, 1922, 17, 473-485 (October).

Brown emphasizes the essentially defensive role of the sympathetic nervous system. It sends the flood of energy toward the exterior, while the parasympathetic nervous system sends it inward. The sympathetic functions in the plane of the subconscious. Pain, fear and anger are the special stimuli which rouse it to action, and when the adequate motor reaction is prevented or restrained, the preparations for defense are thus diverted from their natural purpose and may display a pathologic character of perseveration or dissociation. The restraints of civilization are liable to entail this perversion of a primary defensive mechanism, and this, he reiterates, is the key to the general pathology of the sympathetic nervous system. Among the instances he cites are the almost epidemic appearance of hyperthyroidism after the San Francisco earthquake, after the massacres at Kishineff and during the period of airplane bombing of London. He adds that as the sympathetic is the intermediary between the skin and the endocrine glands and the brain, this explains how the effect of climate on the skin can modify brain functioning. Certain associations of ideas can act on the autonomic nervous system independently of the will. Hence if we can realize this association of ideas voluntarily, the same autonomic reactions may follow.—*J. Am. M. Ass.*, 79, 1961.

(AUTONOMIC NERV. SYST.) Methylene blue, antagonistic to excitants of the PARASYMPATHETICS (*Le Bleu méthallène, antagoniste des excitants parasympathétiques*). Heymans (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 396-398.

Experiments on the hearts of frogs, turtles and dogs demonstrate that methylene blue possesses, although to a less degree than atropine, an action antagonistic to that of muscarine, acetylcholine and arecaline; the action is reciprocal to a certain degree.—*T. C. B.*

Tumors of the CAROTID GLAND (*Gezwellen der glandula carotica*). Nieuwenhuijse, *Nederl. Tijdschr. v. Geneesk. (Haarlem)*, 1922, 66, (II), 2024-2025.

Treatment of DIABETES (*Diabetes-Therapie*). Assmann, *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1665; *Klin. Wchnschr. (Berl.)*, 1922, 1, 2069.

The author recommends treatment of diabetes by restriction of diet, the value of which was proved by the war.—*J. K.*

The effect of INSULIN on experimental hyperglycemia in rabbits. Banting (F. G.), Best (C. H.), Collip (J. B.), Macleod (J. J. R.) & Noble (E. C.), *Am. J. Physiol. (Balt.)*, 1922, 62, 559-580.

"The present investigation was undertaken to obtain further evidence of the scope of the action of insulin by studying its effect on the various experimental conditions that are known to cause marked hyperglycemia in rabbits." The rabbits were of uniform size and breed, and fed several days preceding the experiments on oats and hay, sometimes with sugar added. Blood was taken from the ear and sugar determined by the Schaffer-Hartman method. When the fall in blood sugar was established by injections of insulin, piqure, epinephrin, ether, asphyxia (mechanical or CO) did not cause the usual degree of hyperglycemia; there was sometimes a rise, but not to the level obtaining before insulin was given. Even when insulin was given at the time of experiment, hyperglycemia did not occur, or was greatly diminished.—T. C. B.

Islands of Langerhans free in the connective tissue of an otherwise normal human PANCREAS (*Über frei im Bindegewebe liegende Langerhans'sche Zellhaufen in einem sonst normalen menschlichen Pankreas*). Clara (M.), *Anat. Anz. (Jena)*, 1922, 55, 402-406.

The islands described were found free in the connective tissue of the pancreas, unassociated with the usual parenchyma. In one instance an island was connected to an excretory duct. Independent ducts were frequently seen in the neighborhood of these islands. One interpretation of this unusual condition is that local atrophy of the alveolar parenchyma had occurred, with a persistence of the islands and some of the ducts.—A. T. R.

Influence of PANCREATIC perfusate upon the carbohydrate metabolism of depancreatized animals. Clough (D. C.), Stokes (A. M.), Gibbs (C. B. F.), Stone (N. C.) & Murlin (J. R.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 20, 66-67.

After removal of the pancreas in cats and dogs, results typical of diabetes were obtained. The respiratory quotient, blood sugar, and D/N ratio were studied. Sugar, in the form of dextrose or sucrose, was given through a stomach tube. Pancreatic perfusate was then administered intravenously, subcutaneously, or intraperitoneally. This perfusate was obtained from the pancreases of cats, dogs, pigs, or oxen. There followed a rise in the respiratory quotient, a marked drop in the level of the blood sugar and changes in the D/N ratio. The report contains an outline of the exact methods used.—J. C. D.

Acetone forming microorganisms in the intestinal flora of DIABETICS (*Sur la présence de microbes acétonogènes dans la flore intestinale des diabétiques*). Berthelot (A.) & St. Danysz-Michel, *Compt. rend. Acad. d. sc. (Par.)*, 1922, 174, 1303-1306; abst., *Ber. u. d. ges. Physiol. (Berl.)*; 1922, 14, 274.

Acetone forming microorganisms are rather widely distributed. None was found in the stools of 32 persons who were either healthy or suffering from conditions other than diabetes. In the stools of 22 persons with diabetes of varying degrees of severity, such bacteria occurred in 17 cases. The organisms are not of any single type, but include bacilli, cocci, and others. Many are spore forming; all are highly resistant to acetone. The occurrence of these organisms in diabetics is probably dependent upon the presence of undigested glucose in the intestine. A few of the organisms, when given daily to rabbits, in massive doses, cause glycosuria; others do not.

—E. C. A.

DIABETES, Beta-oxybutyric acid and levulose (*Diabète, acide B-oxybutyrique et lévulose*). Desgrez (A.), Bierry (H.) & Rathery (F.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175, 536-539 (September).

Different sugars are not interchangeable in nutrition. There is a chemical alimentary specificity. Fructose remedies certain metabolic accidents, and in diabetes combats the elimination of oxybutyric acid. When the sugar tolerance of a diabetic is established, fructose should be the sugar given, plus a due supply of phosphates and vitamin B.—*Physiol. Abst.*, 7, 504.

DIABETES MELLITUS together with **DIABETES INSIPIDUS** (*Untersuchungen über einen Fall von gleichzeitig bestehenden Diabetes mellitus und insipidus*). Freund (H.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 1780-1785.

The patient was a man of 36 who had always suffered from polydipsia. His urine was repeatedly analyzed but no sugar was detected until he was 34 years old. He died in coma. Postmortem examination showed that the hypophysis was small and that the veins of the pars anterior were much congested. No other changes were found macroscopically or microscopically. The "thirst test" and the "pituglandol test" gave results typical of diabetes insipidus, but the extraordinary thirst did not disappear, as is usually the case, when pituglandol was injected. The author believes that it is possible that the primary cause of both types of diabetes is situated in the pancreas and quotes the results of many authors who, by lesions of the pancreas, obtained polyuria without glycosuria. There may be an important relationship between the hypophysis and the pancreas. It is more probable, however, that pathological changes simultaneously affect the centers of water and sugar metabolism which are situated near each other in the interbrain.—J. K.

Calcium change in DIABETES (*Contributo allo studio del ricambio del calcio nel diabete*). Galdi (G. F.) & Paxeddu (G. E.), *Folia med. (Napoli)*, 1922, 8, 68-77; 109-120.

Thermal stations and "modern treatment" of DIABETES (Stazioni termali o "trattamento moderno" del diabete). Monod (G.), Arch. med. Hydrol., No. 1 (May); abst., Rassegna internaz. di clin. e terap. (Napoli), 1922, 3, 470-471.

The influence of PANCREATIC extracts upon the carbohydrate metabolism of depancreatized dogs. Gibbs (C. B. F.), Clough (H. D.), Stone (N. C.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 67-68.

The experiments were similar to those given above (Clough et al.), except that an extract of freshly removed dogs' pancreas was used. Extracts given by stomach had very little effect. Intravenous, intraperitoneal, intramuscular, and subcutaneous injections resulted in a marked fall of blood sugar level, the lowest level occurring about 4 hours after the injection, regardless of the route used. The subcutaneous injection method was least harmful to the animal as a whole and proper purification of the extract did away with most of the painful effects at the place of injection.—J. C. D.

Treatment of DIABETES MELLITUS (Behandeling van diabetes mellitus). Hoogslag (W.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, 66 (II), 871-875.

The modern methods of dietetic treatment are shortly reviewed.
—J. K.

Two hundred and fifty cases of DIABETES (Opmerkingen naar aanterding van 250 gevallen van suikerzichte). Hoogslag (W.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, 66, (II), 1934-1951.

A collection of important practical observations—J. K.

Is the yeast treatment of DIABETES logical [Ist die Begründung der Wirkung der Ferment (Hefe) therapie bei Diabetes mellitus zutreffend]? Lenné, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1310-1311.

Some investigators recommend the administration of yeast in diabetes. Lenné thinks this is not logical.—J. K.

(DIABETES) Properties and methods of preparation of the ANTI-DIABETIC substance (glucopyron) generated by the PANCREAS. Murlin (J. R.), Pro. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 70.

The author outlines the essential steps in the preparation of this substance and points out that in alcoholic extracts all the active substance is not found in the final extract. He reviews its physical properties, and calls attention to a paper by Murlin and Kramer,

published in 1916, in which they reported the demonstration of the sugar oxidizing property of aqueous pancreatic extract when given by mouth. He suggests the name, glucopyron, for the active substance however obtained.—J. C. D.

On the relation between ligature of the ductus thoracicus and the tolerance for carbohydrate. Ohara (T.), *Tohoku J. Exper. Med.* (Sendai), 1922, 3, 163-176.

There generally results a protracted hyperglycemia, frequently accompanied by glycosuria. The author regards the condition as due to a part of the pancreatic hormone being secreted into the blood stream via the lymph.—*Physiol. Abst.*, 7, 503.

Prognosis of DIABETIC retinitis as regards life and vision (*Le pronostic vital et le pronostic visuel des rétinites des diabétiques*). Onfray (R.), *Ann. d'ocul. (Par.)*, 1922, 159, No. 8 (August); abst., *Presse méd. (Par.)*, 1922, 30, 859.

Onfray studied 76 new glycosuric subjects with retinitis in addition to the 24 cases already reported by him in the "*Ann. d'ocul.*" in 1918. Among this last group, 7 who died during the first 3 years of his observation had hypertension (maximum 25°, minimum 13°). The patients with well defined Ambard's constant usually survived. True diabetic retinitis did not seem to be so often fatal as the hemorrhagic forms. But prognosis as regards vision is sombre, although complete loss of sight was rare. The visual acuity was so poor in these patients that they could not read, play cards, or even feed themselves.—R. G. H.

Cause and dietetic treatment of severe DIABETES (*Zur diätetischen Therapie der schweren Diabetesfälle und zur pathogenetischen Theorie dieser Erkrankung*). Petrén (K.), *Psychiat. en Neurol. Bl. (Amst.) (Neurotherapie)*, 1921, 25-77.

In diabetes the reduction of the quantity of protein in the diet is as necessary as the reduction of the carbohydrates. A regulated diet is necessary even when the excretion of nitrogen does not exceed 3 to 4 gms. daily. The diet recommended may be given for a long time (in one case 82 days) without symptoms of underfeeding. The patients may even gain weight. The diet consists only of vegetables, fat and butter and blueberries. The author objects to the Allen treatment because in some cases it may produce acidosis, which may even prove fatal, and because the patients lose not only flesh, but strength and energy. In some cases in which the Allen treatment was used the patients did not die of diabetes but of starvation. Allen has stated that after a certain time in severe diabetes the patients cannot support fat. Petrén believes that this is true only when enormous quantities are given and in the last stage when the patients can support nothing. Neurological symptoms of

diabetes, when treatment is given according to Petré's method, rapidly disappear. When the knee jerks are negative they do not come back. A fact peculiar to diabetes is that as soon as the quantity of nitrogen that is excreted exceeds a certain amount acidosis begins. Therefore, Petré's diet, which tends to diminish the excretion of nitrogen, has a splendid effect in acidosis. Another advantage of the recommended diet is that the carbohydrate tolerance may be increased. Even with this diet, however, the prognosis of diabetes remains as bad as before.—J. K.

Los regímenes equilibrados en la DIABETES. Rathery (F.), Arch. de med., cirug. y espec. (Madrid), 1922, 9, 289-294 (November).

A brief general discussion of the factors determining a properly balanced diabetic ration.—R. G. H.

— **(DIABETES)** Relation between the sugar content of blood plasma and cerebro-spinal fluid (*Beziehungen zwischen dem Zuckergehalt des Plasmas und des Liquors*). Ruzsnyák (S.) & Csáki (L.), Biochem. Ztschr. (Berl.), 1922, 133, 355-357.

A series of determinations of the sugar reducing content of blood plasma and cerebro-spinal fluid taken from the same individual at the same time. In both diabetic and non-diabetic subjects the sugar content of the cerebro-spinal fluid is always less than that of the blood plasma, and is about 0.05%. However, it is possible that when sudden changes in blood sugar occur, because of the sluggish change in cerebro-spinal fluid, higher values may be found in the former than in the latter.—F. S. H.

Three months study of the influence of the anti-diabetic substance on a case of severe DIABETES. Sutter (C. C.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 68-69.

Anti-diabetic substance was given through a duodenal tube with good results. At the end of a week the treatment was stopped for three weeks. The blood sugar rose, but not to its previous level. Treatment was resumed in the form of 45 subcutaneous injections continued over a period of 2 months. The blood sugar was kept down, and the sugar, acetone, and diacetic acid disappeared from the urine and did not reappear again when the diet was made more liberal. Administration by mouth was without results. There was little difficulty experienced with the subcutaneous method. Only 3 of the injections gave any definite local reaction.—J. C. D.

Development of real DIABETES from cholelithiasis via the PANCREAS (*Entwicklung eines echten Diabetes aus einer Cholelithiasis auf dem Weg über das Pankreas*). Umber, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1221.

The patient first suffered from cholelithiasis. The urine was sugar free even after ingestion of 100 gm. of glucose. There was no hyperglycemia. A tumor began suddenly to grow in the abdomen with symptoms of a disease of the pancreas. There was no glycosuria and no hyperglycemia. An operation was performed upon the pancreas cyst and gall bladder. About 3 months later the patient complained of thirst and itching. Typical diabetes was found.—J. K.

(ENDOCRINE) The influence of substances from yeast cells and organs on the rapidity of decomposition of substances by polypeptidases, carbohydrases and esterases (Untersuchungen über den Einfluss von aus Hefezellen und Organen gewonnenen Stoffen auf den zeitlichen Verlauf der Spaltung von Substraten durch Polypeptidasen, Karbohydrasen und Esterasen). Abderhalden (E.) & Wertheimer (E.), *Fermentforsch. (Leipz.)*, 1922, 6, 1-26.

Abderhalden prepared from yeast a substance which influences the velocity of alcoholic fermentation. He experimented on the influence of the same substance on the velocity of the decomposition of dipeptids. Optones from the hypophysis, testicles, ovaries and corpus luteum, cholin and adrenalin did not influence the reaction. Optones from the placenta slightly, and from the thyroid and thymus markedly, increased the velocity. The optones from the thymus and thyroid lost their activity after boiling for 20 minutes. When these optones were dialyzed they were separated into two inactive parts, which, when put together, showed their original activity. That part of the optones which dialyzed was not inactivated by the heat; the other part, which was not dialyzable, was destroyed by heat.—J. K.

A case of Recklinghausen's disease with ENDOCRINE complications (Un caso de enfermedad de Recklinghausen con trastornos endocrinos). Andueza (P.), *Med. ibera (Madrid)*, 1922, No. 256, 241-243.

In many cases of Recklinghausen's disease, endocrine complications may be observed, especially thyroid and suprarenal insufficiency. According to Revilliod, Castellino, Pende and Chauffard, etc., opotherapy plays an important part in the treatment of this disease. The author describes the case of a cretin in whom neurofibromatosis was present in the region of the thyroid. In addition to the symptomatology proper to cretinism, there were many small tumors and irregularly distributed pigmentation. Histological study of one of the tumors showed it to be a fibroma. Thyroid opotherapy was instituted. In ten months the endocrine complications were much relieved and the small tumors underwent slow regression, many of them disappearing, while those that remained became much smaller in size.—E. B.

Progressive myopia and ENDOCRINE disturbances (*Miopias progresivas y perturbaciones endocrinas. Contribución a su estudio etiopatogénico*). Argañaraz (R.), *Semana méd.* (Buenos Aires), 1922, 29, 1161.

Ectasis of the posterior (myopia), or of the anterior segment (keratoconus), of the eye is observed at the time of greatest endocrine activity. The subjects present a pluriglandular syndrome and are heredosyphilitics.—B. A. H.

ENDOCRINIDES syphilitiques angio-neurotiques et angio-neurotrophiques. Andry & Chatellier, *Ann. de dermat. et syph.* (Par.), 1922, 3, June; abst., *Presse méd.* (Par.), 1922, 30, 761.

Under the name of "endocrinides syphilitiques" the authors consider those lesions which present no specific structure, which are not dependent upon any one factor, which are not always cured by specific treatment, which are not even specific in the sense that their complex symptomatology depends upon a change which can be determined by any agent except spirocheta. The authors consider Raynaud's disease as an example of "endocrinide syphilitique angio-neurotrophique"; the endocrine glands (thyroid and ovary), influenced by syphilis, affect the sympathetic system. Erythromelia of Pick is, like Raynaud's disease, sometimes of syphilitic origin. However, these two syndromes do not represent pure endocrinopathies; in Raynaud's disease, as in vascular erythromelia and syphiloma, there is also true syphilitic arteritis.—R. G. H.

(ENDOCRINE) Sclerodermia. Bolton (G. C.), *Maandbl. v. specialistische Geneesk.* (Amst.), 1922, 5, 72.

The endocrine organs probably play an important part in the pathogenesis of scleroderma. Often important changes are found in the thyroid (atrophy of the complete organ, degeneration of the follicles, etc.). In some cases changes in the hypophysis have been found. Though changes in the adrenals have not been described, combination of Addison's disease and scleroderma are known. Bolton theorizes to the effect that insufficiency of the chromaffin system with a diminished tonus of the sympathetic may be an explanation of scleroderma. The low tonus of the muscles of the blood vessels will cause dilatation of the large vessels, especially the veins in the lungs and abdomen, and these vessels will contain large quantities of blood. This, the author believes, combined with the low blood pressure, produces defective circulation in the periphery of the body. Several French authors (Hallopeau, Brissaud) believe that scleroderma is caused by an anatomical lesion of the sympathetic, especially the centers (e. g., the vasomotor center of the floor of the third and fourth ventricles). Bolton believes that this is possible, especially since such tumors could cause a decrease in the production of adrenalin.—J. K.

ENDOCRINE disturbances by thallium (*Weitere experimentelle Ergebnisse über endokrine Störungen durch Thallium*). Buschke (A.) & Peiser (B.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 2182-2184.

When thallium is given to tadpoles growth as well as metamorphosis is retarded. When thymus is added to the thallium retardation of metamorphosis is almost neutralized, but growth remains retarded. In this way dwarf frogs are formed. Thallium seems to produce only functional changes in the endocrine organs, as even severe changes in growth soon disappear after stopping the administration of this metal.—J. K.

New evidence for sympathetic control of some INTERNAL SECRETIONS. Cannon (W. B.), *Am. J. Psychiat. (Balt.)*, 1922, 2, 15-30.

An address, in which the author reviews the work done in the Harvard Physiological Laboratory on the innervation of the adrenal medulla (see *Endocrinol.*, 1922, 6, 277), of the liver as an organ discharging a cardio-accelerator and a pressor agent (see *Endocrinol.*, 1922, 6, 554), and of the thyroid gland (see *Am. J. Physiol.*, 1922, 60, 476). The author then discusses the nature and location of the central nervous control of these organs and the application to human beings of the results of studies on lower animals. He also considers the bearings of these considerations on the character of emotional reactions.—Author's Abst.

Physical therapy in the light of ENDOCRINOLOGY. Chelmonski (A.), *Polska Gaz. Lekarska (Lemberg)*, 1922, 1, 534 (June); cit., *J. Am. M. Ass. (Chicago)*, 79, 1808.

(ENDOCRINE) Pluriglandular thyroid and kidney therapy (Prodotti opoterapici associati). Coronedi (G.), *Terapia (Milano)*, 1921, 11, 8-12 (March),

A résumé of data indicating a functional relation between the thyroid and the kidney, and supporting the utility of "renothyroid" therapy.—Author's Abst.

(ENDOCRINE) Clinical importance and cause of experimental glycosuria in pregnancy (Ueber den diagnostischen Wert und die Aetiologie der experimentellen Schwangerschaftsglycosurie). Dietrich (H. A.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 1403-1407.

The Frank-Nothmann test for the diagnosis of pregnancy is positive in 85% of the cases. Since the glucose used by Frank and Nothmann is very expensive, the author recommends the use of artificial honey, which gives the same results. The influence of adrenin on sugar metabolism in pregnancy has been studied, with the conclusion that when the injection of 1 cc. of adrenin 1:1000 is followed by glycosuria pregnancy exists. Dietrich was able to prove that this test is absolutely unreliable. He states that glycosuria in

pregnancy is not renal glycosuria, as real hyperglycemia is always found; it is an alimentary glycosuria with a lowered tolerance for carbohydrates, perhaps caused by the changes during pregnancy in the hypophysis, liver and thyroid.—J. K.

Functional diagnosis of the diseases of the ENDOCRINE organs (Funktionelle Diagnostik der Erkrankungen des BlutdrüSENSYSTEMS). Falta (W.), Ztschr. f. ärztl. Fortbild. (Jena), 1922, 19, 417-427.

A general review.—J. K.

Psychiatry and ENDOCRINE organs (Psychiatrie und innere Sekretion). Fischer (H.), Klin. Wchnschr. (Berl.), 1922, 1, 2401.

Abstract of lecture.—J. K.

(ENDOCRINE) Methods and purposes of the modern investigations on rickets (Wege und Ziele der neueren Rachitisforschung). Freudenberg (E.), Klin. Wchnschr. (Berl.), 1922, 1, 1422-1425.

Postulates endocrine deficiency as one cause.—J. K.

El cancer y su origen ENDOCRINICO. Guzman (Z), Prensa méd. argentina (Buenos Aires), 1922, 9, 175.

It is claimed that cancer may be caused by interruption of endocrine balance.—B. A. H.

(ENDOCRINE) Importance of Abderhalden's reaction in psychiatry (Die Bedeutung der Abderhaldensche Reaktion für Psychiatrie). Kastan (M.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1191.

In maniac-depressive psychosis 11% showed a positive reaction of Abderhalden with brain; 14% with sexual glands. In dementia praecox, out of 87 cases 27 showed a positive reaction with thyroid; 60 with sexual glands; 30 with brain; 12 with the three organs. In epilepsy 33% had a positive reaction with brain. In dementia paralytica 40% had a positive reaction with brain. In some cases of dementia praecox Steinach's rejuvenation experiment was tried. The serological reactions remained unaltered by the operation. No clinical details are given.—J. K.

(ENDOCRINE) Active principle of organ extract. Kuboto (S.), Nat. M. J. China (Shanghai), 1922, 8, 185-191 (September).

Extracts of lung, spleen and pancreas, when injected intravenously into the cat, lower the blood pressure. They also cause marked contraction of the isolated uterus of the virgin guinea pig. Both these reactions closely resemble the action of histamine. The author was able to isolate from these tissues a substance giving typical chemical reactions of histamine, and physiologically indis-

tinguishable from it. It causes a fall in blood pressure in the cat and a rise of blood pressure in the rabbit (urethane anesthesia), when injected intravenously. It stimulates the isolated uterus of the virgin guinea pig and relaxes the uterus of the rat. Both it and histamine, when injected intravenously into guinea pigs or rabbits, produce respiratory disturbance, cyanosis, tremor, cramps and collapse. The conclusion is therefore drawn that "at least one of the active principles of organ extract is histamine."—L. G. K.

(ENDOCRINE) Three cases of abnormal growth (Drei Wachstumsstörungen). Kundraditz, Wien. klin. Wchnschr., 1922, 35, 663.

The author first reports a case of infantile gigantism with symptoms of acromegaly. The case of a girl of 13 with myxedematous symptoms is also reported. She was about 30 cm. shorter than normal. The skin was dry, with pseudolipomas in the fossae supraclavicularis. The thyroid was not palpable. Her intelligence was comparatively good. Injection of 1 mg. of adrenalin was not followed by glycosuria and produced even a fall of the blood sugar. The case was diagnosed as congenital hypoplasia of the thyroid. Thyroid extract brought about improvement. A boy of 8 years is described. He was shorter than normal and looked like a cretin. There were only some very slight symptoms of rickets. The skin was dry. Radiography showed normal ossification. The thyroid was not palpable, the very small scrotum was empty, and the child was mentally deficient. This case was diagnosed as pluriglandular insufficiency with special dysfunction of the hypophysis. That hypopituitarism was present was proved, according to the author, by the hypoplasia of the gonads, the glycosuria that was sometimes found and the adiposity of eunuchoid type.—J. K.

ENDOCRINE adiposity. Loewy (A.) & Zondek (H.), Ztschr. f. klin. Med. (Berl.), 1922, 95, 282-292.

An illustrated report of 7 cases of adiposity. The type as described here is found only in females and is characterized by the excellent results obtained with thyroidin. Although the patients became much thinner they did not lose their fat where it was most marked and disagreeable. Basal metabolism determinations were of clinical importance only in that they showed that all cases of pathological adiposity are not caused by disturbed metabolic energy. These cases are somewhat similar to cases of hypodystrophy. In some of these the changes in water metabolism are very important, especially when determined by Volhard's method. Thyroidin always raises the respiratory metabolism.—J. K.

Epilepsia y glándulas de SECRECION INTERNA. Malamud (T.), Prensa méd. argentina (Buenos Aires), 1922, 9, 97.

Endocrine disorders often have a part in epilepsy. Certain troubles are perhaps due to the diencephalon.—B. A. H.

(ENDOCRINE) Osteitis fibrosa. Nagelsbach & Westhnes, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1599.

He showed many "endocrine symptoms," details of which are not given.—J. K.

A short note on a patient who died of general osteitis fibrosa. (ENDOCRINE) The critical age of man (*La edad critica del hombre*). Navarro (A.), Prensa méd. argentina (Buenos Aires), 1921, 7, Nos. 12, 13, 14, 15, 18, 19, 20, 22, pp. 146, 159, 172, 183, 220, 234, 244.

A philosophic and scientific exposition on the present and future life and on old age. The author is inspired especially by the work of Marañon and Steinach. He gives in detail the influence of different endocrine glands on the life of man. Several clinical cases are interpreted to agree with these theories.—B. A. H.

(ENDOCRINE) Morphological studies of the lipid substances in starved animals (*Zur Morphologie der lipoiden Substanzen im Hungerzustande*). Okuneff (N.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1922, 71, 99.

Okuneff studied the distribution of isotropic and anisotropic lipoids in the various organs of 6 rabbits starved from 9 to 17 days, during which time the average loss in body weight was 40%. He observed, as many others have noted in other animals, that the weight of the suprarenal glands during hunger was often even doubled. He found that the cholesterol ester content of the suprarenal cortex in starvation was distinctly increased. No noteworthy changes in the cell lipoids were observed in the kidney, thyroid, parathyroids, pancreas, testes and hypophysis. A very great increase in both isotropic and anisotropic lipoids was found in the thymus gland. Whether the deposition of lipoids in these tissues during hunger is primary or secondary to the hunger lipodemia cannot be stated.—D. M.

ENDOCRINE glands and the blood (*Les glandes à sécrétion interne et le sang*). Perrin (M.) & Hanns (A.), Progrès. méd. (Par.), 1922, 37, 537-538.

A brief review.—F. S. H.

Parabiosis in research on ENDOCRINE GLANDS [*Nuevo método para el estudio experimental de la influencia de las glándulas de secreción interna en el desarrollo del organismo (hiperfunción; estudio teórica)*]. Rubinstein (D.), Semana méd. (Buenos Aires), 1921, 28, 477.

To find the influence of the hypophysis on growth the author first combined two young dogs in parabiosis. Later the hypophysis was extirpated from one of the dogs, which caused hypophyseal hypertrophy in the other. The dogs were then separated. The one with the hypertrophied hypophysis presented symptoms of hyperpituitarism. One experiment was performed.—B. A. H.

El cancer y su origen ENDOCRINO. Stajano (C.), Prensa méd. argentina (Buenos Aires), 1922, 9, 265.

Cancer is said to be caused by nervous disorder, influenced by endocrine factors.—B. A. H.

ENDOCRINE organs and avitaminosis. Thomas, Klin. Wchnschr. (Berl.), 1922, 1, 2165.

A short note. The animals were fed a vitamin free diet. After death, hemorrhages, hyperemia and pigmentation with hemosiderin were found in all endocrine organs.—J. K.

Morphological variations of ENDOCRINE origin (Contributo allo studio delle dismorfie endocrine). Vidoni (G.), Arch. di antrop. crim. [etc.] (Torino), 1921, 41, 438-457, 545-571; abst., Ber. u. d. ges. Physiol. (Berl.), 1922, 14, 250.

The variations in appearance and behavior due to disorders of endocrine functions are discussed, and especially the facial angle and its importance from the point of view of criminology and anthropology. The author attempts a classification of skull and face forms (those in acromegaly, myxedema, cretinism, geroderma, exophthalmic goiter, eunuchoidism, mongolism, the adenoid facies and those of tetany and of Addison's disease). Endocrine disorders are manifested also in the build of the body (size, proportions, fat distribution, pigmentation, distribution of hair and appearance of the nails). The form of the nose and of the ear may be affected by endocrine factors, as may also the condition of the teeth (the falling out of the teeth in exophthalmic goiter, the delayed development of the teeth in thymus insufficiency).. Reference is made to the enamel defects in epilepsy. Sexual anomalies are discussed at some length. A case of *pubertas praecox* is reported in a 12 year old imbecile in whom hyperfunction of the testis with accompanying hydrocele is claimed to have a causative relation. The paper ends with a discussion of the possible relations of the endocrine organs to deformities and degenerations in general.—E. C. A.

(ENDOCRINE) Theoretical and practical importance of the endothelial symptom (Zur Theorie und praktischen Verwendbarkeit des Endothelsymptoms). Vogt (E.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1007.

The so-called "retico-endothelial system" consists of the "Kupfer" cells; the reticulum cells in the red pulp of the spleen, the lymph glands, and the bone marrow; and in special parts of the connective tissue of the skin, lungs and serosa. This system is very important, especially in the pathology of the blood. It is considered as the seat of haemoglobin and cholesterol metabolism. This last process is, however, changed in pregnancy. The reticulum cells form the "fibrin ferment" and thus play a very important part in blood clotting. Another function is the maintenance of normal tonus of the walls of the blood vessels. When this tonus is too low, stasis of circulation in the forearm, e. g., by an elastic bandage, is followed by extremely small capillary hemorrhages in the skin ("positive endothelial symptom"). In normal persons this symptom is negative, but during menstruation and pregnancy it is positive. In the menopause also, whether caused by ablation of the ovaries or by x-rays, or whether it is quite natural, a positive endothelial symptom is found. The author concludes that physiological changes in the endocrine organs of women (as during menstruation, pregnancy, etc.) give rise to a positive endothelial symptom. The positive symptom after hysterectomy is explained as being due to the supposed endocrine function of the uterus.—J. K.

(ENDOCRINE) Organotherapy in neuroses and psychoses (*Organotherapie bei Neurosen und Psychosen*). Wagner-Jauregg, Wien. klin. Wchnschr., 1923, 36, 1-4.

A general uncritical review.—J. K.

Basal metabolism after ingestion of sugar in ENDOCRINE disturbances (*Das Verhalten der Standardumsatzsteigerung nach Zuckerzufuhr bei endokrinen Störungen*). Weisz (R.) & Adler (E.), Klin. Wchnschr. (Berl.), 1922, 1, 1592-1595.

In normal individuals ingestion of saccharose raises the basal metabolism 9.9% to 12.7%. In a patient with Graves' disease this raise was 64.4%. In a case of myxedema it was 26.3%, but thyroidin caused diminution to normal.—J. K.

(ENDOCRINE) Experimental studies on the importance of organotherapy (*Experimentelle Untersuchungen über den Wert der Organotherapie*). Zondek, Klin. Wchnschr. (Berl.), 1922, 1, 1668.

Decomposed products of endocrine glands showed no specific endocrine action. These specific reactions are obtained only by grafts or by administration of extracts which have not undergone chemical changes.—J. K.

(GONADS) Definition and classification of the sexual characters of the Urodela (*Définition et classification des caractères sexuels des Urodèles*). Aron (M.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 246-247.

Formation and action of TESTICULAR harmozone in the Urodela
(Conditions de formation et d'action de l'harmozone testiculaire chez les Urodèles). Aron (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 248-250.

The intensity of the manifestations of rut in the Urodela depends on the quantity of harmozone thrown into the organism and the continuity of its action. Secondary sexual characters are unequally susceptible to the action of testicular harmozone.—T. C. B.

(GONADS) **The OVARY in different psychoses** (Contribution à l'étude de la glande ovarienne dans les différentes psychoses). Ballif (C.), *Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy*, 1921, 3, 20-22 (September).

The ovaries of 31 psychotic individuals were studied histologically. The greatest amount of lipoids was found in 2 cases of myxedema. The distribution extended not only through the corpora lutea but also into the primary follicles and the ovisacs. Similar distribution was found in a case of anxious melancholia with a goiter. The amount of lipoids was very much diminished in cases of dementia precox, senile dementia, in some cases of pellagra and a case of non-goitrous melancholia. Where confusional states existed, in mania or epilepsy, a normal picture was observed.

—F. S. H.

(GONADS) **A case of pseudohermaphroditismus masculinus**. Benda, *Klin. Wchnschr. (Berl.)*, 1922, 1, 2499.

(GONADS) **The TESTES in general diseases with particular reference to the changes in the interstitial cells** [Die Hoden bei Allgemeinerkrankungen (mit besonderer Berücksichtigung des Verhaltens der Zwischenzellen)]. Berberich (J.) & Jaffe (R.), *Frankfurt. Ztschr. f. Path. (Weisb.)*, 1922, 27, 395.

A study was made of the testes of one hundred subjects divided as follows: 21 dying of acute illness, 17 to 56 years of age; 50 dying of chronic diseases, 17 to 56 years of age; 6 dying of acute illness, 56 years of age and over; 20 dying of chronic diseases, 56 years of age and over; 2 cases of undescended testis; 1 case of unilateral castration coming to autopsy one year after operation; and 9 cases of fibrosis testis—also included under acute and chronic diseases. The authors used frozen sections stained with fat stains and paraffine sections stained with hematoxylen and eosin. Some of the important observations follow. In young individuals dead of acute diseases there rarely was any injury to spermatogenesis, while the interstitial cells were generally more or less increased. In old men dying of acute diseases, spermatogenesis was usually considerably impaired, and usually very few interstitial cells were present. In chronic diseases in young individuals, no constant changes were found.

About one half of the cases showed impairment of spermatogenesis. The interstitial cells were numerous in those dying of cachexia. In old individuals injury to spermatogenesis was generally a constant finding, but the interstitial cells were rarely significantly increased. The authors could not show any definite relation between the definite diseases and changes in testes. Concerning the "Fettrandzone" of the Sertoli cells, and the lipoid content of the interstitial cells, the authors observed that when the interstitial cells were rich in lipoid, the Sertoli cells were poor, and vice versa.—H. L. J. (D. M.)

(GONADS) The existence of an ovarian gland homologous to the interstitial gland of the testis (*Sur l'existence d'une glande ovarienne homologue de la glande interstitielle testiculaire*). Berger (L.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175 (September); *abst., Presse méd. (Par.)*, 1922, 30, 967.

The paraganglia of the ovarian hilum are homologous with the accumulation of localized cells in the sympathetic nerves of the testicular hilum, the albuginea, or their vicinity. The paranervous accumulation of the testicle is connected with the interstitial elements and their process of development is the same. While the large paraganglion masses in the testicle make investigation difficult, their scarcity in the ovary permits easier study. The author concludes that since there are paraganglionic elements in the ovary, it is probable that the interstitial gland of the testicle is also to be considered as a paraganglion.—R. G. H.

(GONADS) The action of the internal secretion of the TESTIS and PROSTATE upon metabolism. Bogoslovsky (G. N.) & Korenchevsky (V. G.), *Russ. J. Physiol.*, 1921, 3, 48-54.

The nitrogen and the gas metabolism were studied in normal and castrated dogs before and after injections of fresh emulsions of the testicles and of the prostate. Both had a much more marked effect on castrated animals. Both emulsions cause an increase in the N metabolism, which may rise in castrated animals, in some cases by 18.9% above that before castration. No definite changes in the gas metabolism were observed. The diuresis is decreased in castrates treated with the testicular emulsion, but in thyriodectomized castrates it is generally increased. Prostate emulsions increase the diuresis; this is more marked in castrates. The general conclusion is that the testicle and the prostate are synergetic glands of internal secretion.—*Physiol. Abst.*, 7, 449.

(GONADS) Hydrocephalus with obesity (*Hydrocéphalie avec obésité*). Bonnet, Babanneix & Carrette. *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, 46, 1723-1731.

A case of probable ovarian insufficiency in which adiposogenitalis was due to congenital syphilis.—F. S. H.

(GONADS) CORPUS LUTEUM extract in hyperemesis gravidarum (L'extrait de corps jaune contre les vomissements de la grossesse). Cheinisse. Presse méd. (Par.), 1921, 29, 306 (April).

The author points out that it is about fifteen years since M. G. Stella proposed the treatment of pernicious vomiting of pregnancy with ovarian extract. He says that in the last few years ovarian therapy has been taken up in the United States and France by more precise methods, namely, the injection of extract of corpus luteum. The intramuscular and intravenous use of the extract has given favorable results. It is usually productive of no harm but should not be used in goitrous women.—Am. J. Obst. & Gynec., 4, 450.

(GONADS) A case of true lateral HERMAPHRODITISM in a pig with functional OVARY. Corner (G. W.), J. Urol., 1921, 5, 481-485.

The specimen described was found among several brought from a slaughter house, so the nature of the external genitalia could not be determined. The specimen itself showed a *normal uterus*. The left tube and ovary were normal and functional. Corpora lutea were found in the latter and a recently discharged ovum was found in the tube. Sections showed normal ovarian tissue without any trace of testicular tissue. On the right side, the uterine horn ended in a slender tube which became very small and disappeared in connective tissue near the epididymus. At the site of the ovary on this side was a testis, normal in appearance and size. Sections showed normal tubular and interstitial tissue but no spermatozoa. The epididymus, which was normal in appearance, was continued down parallel with the horn of the uterus as the Wolffian duct. This is the first case of true hermaphroditism in swine in which there is absolute proof of the functioning of one of the gonads.—J. C. D.

(GONADS) Experiments on genital hormones (Essai d'expérimentation sur les hormones génitales). Cotte (J.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 842-844.

An attempt to prove the presence of genital hormones on the hypothesis of antigen-antibody. If there is a conflict between hormones, which prevent, for example, the development of a testicle grafted into a female, and if the hormones are colloidal, there may be a production of antibodies under the influence of hormones of the graft. The grafted female would be in some ways anti-male, and might give birth only to females. Female guinea pigs were grafted with a testicle and allowed to breed. The reverse operation was also performed. No positive results were obtained. The female gave birth to both male and females.—T. C. B.

the sexual cords in the form of clusters of luteal cells were also found in the testes of young birds of breeds other than the Sebright.
—W. J. A.

(GONADS) The origin and histogenesis of epithelioma of the adult TESTICLE in man (*Sur l'origine et l'histogénèse de l'épithélioma séminifère du testicule adulte chez l'homme*). Peyron (A.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 842.

A demonstration, the communication to be published later.
—T. C. B.

(GONADS) The "all or none" law and gynandromorphism in birds (*La loi du "tout ou rien" et le gynandromorphisme chez les oiseaux*). Pézard (A.), *J. de Physiol. et de path. gén. (Par.)*, 1922, 20, 200-211.

Various operations (total or unilateral castration, or castration followed by implantation of minute fragments of testicle) were performed on young Leghorn cocks at the time when secondary characteristics began to appear. At autopsy after full development widely different amounts of testicular tissue were present. Nevertheless, in the series of animals there were only two types, as judged by growth of the comb, the wholly sexed and the wholly neutral, without intermediate forms. The rate of growth of the comb was independent of the amount of active testicular tissue; and its decrease in size after castration was not affected by the presence of small testicular nodules. If the nodules became effective in inducing a renewed growth of the comb, the normal curve of resumed growth started at once and without transition from the period of regression. The "all or none" law, therefore, applies to the male characters, but the minimal effective amount of testicular tissue may not be the same for all. The secondary sex characters of the hen seem to obey the same law.—W. B. C.

(GONADS) Dercum's disease and OVARIAN opotherapy (*Contributo allo studio della malattia di Dercum e opoterapia ovarica*). di Poggio (E.), *Rassegna di clin., terap. [etc.] (Roma)*, 1922, 21, 129-135.

The author has obtained good results in the treatment of a case of Dercum's disease with ovarian extract.—G. C.

(GONADS) Pseudohermaphroditismus masculinus internus with transverse displacement of the TESTIS (*Zur Kenntnis des Pseudohermaphroditismus masculinus internus mit "Dystrophia transverse testis"*). Priesel (A.), *Frankfurt. Ztschr. f. Path. (Weisb.)*, 1921, 26, 80.

The case is reported of a man, aged 77 years, who died of symptoms of scurvy. At autopsy in an otherwise normal individual

there was found a persistence of the Mullerian ducts which had become differentiated into Fallopian tubes, uterus and vagina.

—H. L. J. (D. M.)

(GONADS) Function of the interstitial cells of the TESTICLE (Die Funktion der zwischenzellen des Hodens). Raffé (R.), Klin. Wchnschr. (Berl.), 1922, 1, 1482.

When spermatogenesis is disturbed the interstitial cells may be increased or decreased in number. The interstitial cells have a trophic as well as an endocrine function, but of these functions nothing is known with certainty.—J. K.

(GONADS) Steinach operation for dementia praecox (Contribución al estudio de la demencia precoz. El tratamiento de la demencia precoz por el método de Steinach para las tituladas curas de rejuvenimiento). Raitzin (A.), Semana méd. (Buenos Aires), 1922, 29, 1238.

In two cases of catatonic dementia praecox the Steinach operation was performed. The mental condition was not improved. One of the patients died, 7 months after the operation, of tuberculosis.

—B. A. H.

(GONADS) Modifications determined by x-rays in the rabbit's OVARY (A propos des modifications déterminées par les rayons X dans l'ovaire de la lapine). Regaud (C.) & Lacassagne (A.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 938-940.

A reply to Salazar (Compt. rend. Soc. de biol., 1922, 87, 703).

—T. C. B.

(GONADS) Homosexualiteit. Rogge (H. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, 66 (II), 1068-1075.

General article.—J. K.

(GONADS) TESTICLE transplantation (Ueber die neueren Bestrebungen der Hodenverpflanzung). Rosenthal (O.), Med. Klin. (Berl.), 1922, 18, 370-371.

Criticism of the custom of unilateral transplantation of testes. The author believes that the operation may eventually cause a concealed malady or a trauma in the man from whom the testis is taken. The likelihood of immoral commerce in testicles is given as another argument against this practice.—A. B.

Irradiation of the OVARY of the rabbit: the law of radiosensibility of Bergonié and Tribondeau (A propos de l'irradiation de l'ovaire de la lapine: quelques doutes au sujet de la loi de radio-sensibilité de Bergonié et Tribondeau). Salazar (A. L.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 703-705.

Histological and critical.—T. C. B.

(GONADS) Sex glands of mammals. II. Resection of the vas deferens (*Études expérimentales sur les glandes sexuelles chez les mammifères. II. Expériences sur la résection du "vas deferens"*). Sand (K.), J. de Physiol. et de path. gén. (Par.), 1921, 19, 494-503.

Resection of the vas deferens before puberty is without influence, and thereafter it affects testicular structure only slowly; six months or a year may be required before effects are seen. Transection is equivalent to resection. Unilateral resection with contralateral castration results in extreme tubular atrophy and extraordinary hypertrophy of the Leydig cells, which favors the theory that they are the source of male sex hormones. Sex characters developed normally in all cases and sex activity was marked, though there was almost total tubular atrophy. The animals used were rabbits, guinea pigs and rats.—W. B. C.

(GONADS) Röntgen ray castration in man (*Ein Beitrag zur Röntgen-Kastration beim Mann*). Schinz (H. R.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 886-889.

A review of the application of Röntgen rays to castration of man. Four cases from the literature and one case observed by the author are cited. The relative dosage for temporary and total castration for men and women is given.—A. T. R.

(GONADS) Steinach Operationen. Schreiber (F.), Beitr. z. klin. chir. (Tübing.), 1922, 127, 212-213.

Report of 4 cases. One was a very senile man of 65 with arteriosclerosis and polyneuritis. The only effect of the operation was three erections after ligation of the vas deferens. A man of 67 had arteriosclerosis and apoplexy. He had one erection after the Steinach operation, but no other improvement. The third case was a very senile man with trigeminal neuralgia. There was no improvement after the operation. A homosexual patient was castrated and a cryptorchid testicle, which was completely changed into connective tissue, was transplanted from a boy of 16. After a period of 15 months he showed only pederastic symptoms he said he felt some heterosexual inclination but remained impotent.—J. K.

(GONADS) Effect of castration in epidemic encephalitis (*Ueber die Wirkung der Kastration bei epidemischer Encephalitis*). Stern (F.), Klin. Wchnschr. (Berl.), 1922, 100, 15.

Report of 2 cases. One was a man who 2 years before had had some amyostatic symptoms in the head, neck and left arm. After castration he remained in the same condition. One and a half years later his voice and soon consider-

able growth of the gonads (penis 11 cm. long, testes like walnuts), abundant growth of hair on the trunk and pubic region and development of a mustache. Masturbation and pollutions occurred. Spermatozoa were found. In the previously intelligent child psychological changes set in. He became restless and incompatible. There was no psychic prematurity sexually. Considerable increase of lymphatic and eosinophile cells was noted in the blood. No tumor of testis or adrenal cortex could be determined. The author concludes, according to the well-known theories of a connection between hypopinealism and pubertas praecox (especially in hypoplasia of the pineal, Askanazy and Brack), that there was direct damage of the pineal through the inflammatory products of encephalitis, thus causing hypofunction and sexual prematurity.—A. B.

(GONADS) Organotherapy in OVARIAN hemorrhage (Klinische untersuchungen über den Wert der Organotherapie bei ovariellen Blutungen). Stickel (M.) & Zondek (B.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.), 1922, 85, 83-106.

Unsatisfactory and contradictory results were obtained.

—F. S. H.

(GONADS) Sex and age (Geschlecht und Lebensalter). Straatz, Klin. Wehnschr. (Berl.), 1922, 1, 1668.

The influence of the secondary sexual characteristics on the body are due only in a small degree to endocrine influences. The authors believe that these characteristics are influenced most of all by heredity.—J. K.

(GONADS) On a case of eunuchoidism. Sumiwo (S.), Chyugwai Iji-Shimpo, 1922, 42, No. 1011; No. 1012 (May); cit., Jap. Med. World, 2, 303.

(GONADS) Corpus luteum and ovariectomy during pregnancy. Szymanowicz (J.), Polska Gaz. Lekarska (Lemberg), 1922, 1, 554 (July); cit. J. Am. M. Ass., 79, 1808.

(GONADS) Genital infantilism. Wohlaue, Klin. Wehnschr. (Berl.), 1922, 1, 1626.

A man of 18 with well developed crines pubes, undescended testicles, important changes in teeth and skull (no more details as to the changes are given) and symptoms of tetany (positive Chvostek and Erb symptoms). The relation of latent tetany and hypofunction of the gonads is probable, as is shown by the studies of Melchior.

—J. K.

(GONADS) Steinach operation (Wann und wie ich ohne Erfolg gesteinacht wurde). Zeissl (M.), Wien. klin. Wehnschr., 1922, 35, 764-765.

The author suffered from hypertrophy of the prostate. Vasectomy on both sides had no effect. The rejuvenation which, according to Steinach, should follow this operation was not seen. The author considers the Steinach operation useless.—J. K.

(GONADS) The effect of x-rays on the internal secretion of the OVARY (*Experimentelle Untersuchungen über die Beeinflussung der inneren Sekretion des Ovariums durch Röntgenstrahlen*). Tsukahara (I.), *Ztschr. f. Geburtsch. u. Gynäk.* (Stutt.), 1922, 85, 36-48.

When both ovaries are removed from rabbits a hypersensitivity to adrenin is found, as is shown by a hyperglycemia which lasts for some hours after doses of usual ineffectiveness. This sensitivity is at a maximum 2 months after castration. A bilateral administration of the castration x-ray dose on the ovaries brings about the same sensitivity. The follicular apparatus is damaged, the ripening follicle being harmed the most. The castration dose produces no changes in the uterus. The eosinophil cells of the hypophysis are greatly increased.—F. S. H.

(GONADS) Present status of knowledge of MENSTRUATION (*Der heutige Stand der Lehre von der Menstruation*). Seitz (A.), *Med. Klin.* (Berl.), 1922, 18, 1013-1017 (August).

A short review of the newer knowledge of menstruation, especially from the standpoint of the histological cycles in the endometrium and the ovary.—E. N.

Sclérodémie et HYPOPHYSE. Bénard (R.) & Coulaud (E.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1922, 46, 1518-1524.

Brief bibliographic review.—F. S. H.

ADIPOSO HYPOPHYSEAL syndrome following epidemic encephalitis (*Sindrome adiposo-ipofisaria consecutiva ad encefalite epidemica*). Bertolani (A.), *Riv. di patol. nerv.* (Firenze), 1922, 27, 72-74.

Report of the cases of two women with adiposo hypophyseal syndrome following epidemic encephalitis. It might have been a question of an inflammatory atrophy of the hypophysis after infection, as reported by Massalongo and Piazza, or it might have been due to inflammatory lesion of the gray substance of the infundibulum and that below the floor of the third ventricle. The author believes in what he calls a mixed theory, that a primitive lesion of either may have interrupted the interrelation between the pituitary and some nervous centers.—G. V.

(HYPOPHYSIS, GONADS). A pluriglandular syndrome following influenza (*Su un cas di sindrome pluriglandolare consecutiva ad influenza*). Bosisio (R.), *Folia med.* (Napoli), 1922, 8, 394-400.

Report of a girl who, after influenza, presented various symptoms which led to a diagnosis of hypophyseal and gonadal insufficiency.—G. C.

HYPOPHYSEAL dwarfism (*Nanismo hipofisaria de Aschner-Paltauf*). Castex (M. R.) & Waldorp (C. P.), *Rev. Asoc. méd. argent.* (Buenos Aires), 1921, 34, 47-68; *Semana méd.* (Buenos Aires), 28, 564.

A report of two cases. The subjects were dwarfs, with well developed genital organs, the intelligence of adults, and small sella turcicas. In one case there was anterior hypopituitarism, plus polyuria. The two patients were heredosyphilitic.—B. A. H.

The secretory cycle of the cells of the **HYPOPHYSIS** (*Sur le cycle sécrétoire de la cellule hypophysaire*). Collin (R.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 549-551.

Histological.—T. C. B.

Extracts of **HYPOPHYSIS** and blood coagulation (*Etude sur l'action des extraits d'hypophyse sur la coagulation sanguine*). Feissly (R.), *Presse méd. (Par.)*, 1922, 30, 997-998.

Feissly investigated whether the increased coagulation of the blood following the use of extracts of the posterior lobe of the hypophysis was to be attributed to some specific substance contained in the gland, or to substances occurring also in extracts of other tissues. Extracts were made from various organs either by simple maceration without heating, or by maceration followed by heating in an acid medium. Experiments with these extracts as well as with pituglandol, pituitrin, luteoglandol, splenoglandol and even with the autitrine of Parke Davis (an extract made of the anterior lobe of the hypophysis) produced acceleration of the blood coagulation in vivo. The changes in coagulability were determined with the very delicate instrument devised by Feissly. The results were checked by Fonio's method, which is based on an entirely different procedure. The extracts obtained by simple maceration were found to possess strongly thromboplastic properties both in vitro and in vivo; the boiled extracts, on the other hand, gave no evidence of thromboplastic activity in vitro, yet they increased coagulability in vivo, showing that coagulation must be connected with some kind of reaction within the organism. No increase of prothrombin or decrease of anti-thrombine could be demonstrated, but a definite and powerful enzyme action was observed. The effect of extracts on man were studied, special attention being given to the duration of increased coagulability and the occurrence of a phase of decreased coagulability. Blood samples were taken at intervals of 13 minutes, 1 hour and 7 hours after injection of the extracts. A certain degree of increased coagulation was found, which occurred also in

vitro and was more marked in plain glass tubes than in paraffin-coated ones; but very definite decrease of coagulation followed; both phenomena seemed entirely independent of the blood pressure which always rose one-half hour after injection. Feissly warns against the indiscriminate use of such extracts and calls attention to the fact that peptones are known to produce a very distinct anti-thrombine reaction in dogs and none in rabbits. Non-boiled extracts tend to increase the blood pressure; boiled extracts lower them unmistakably. In the main the boiled extracts act like very weak solutions of peptones; the changes in the blood pressure can be obviated by giving them subcutaneously, whereas intravenous injection produces severe reactions; a second subcutaneous injection, given 2 hours after the first, again produces well-marked increase in the coagulability of the blood. While all of these extracts are physiologically active—and powerfully so—there is no evidence that the increase of blood coagulability can be ascribed to pituitary extracts alone.—G. L.

(HYPOPHYSIS) The control of pituitary lesions, as affecting vision, by the combined surgical, x-ray, radium treatment. Frazier (C. H.), Arch. Opth. (New Rochelle, N. Y.), 1921, 50, 217-226.

The first part of the paper is taken up with a consideration of the operative methods, their disadvantages and unsatisfactory results. The author emphasizes the frequency with which the early eye defects in hypophyseal cases are overlooked. Four cases are reported in which the use of radium and x-ray following operation prevented or delayed the return of the symptoms. Three of these were subsellar decompressions. One case has a history covering 4 years since operation. The author points out that more evidence is needed. He recommends subsellar decompression followed by x-ray and radium. The removal of the floor of the sella enables these agents to act more directly on the tumor.—J. C. D.

(HYPOPHYSIS) Nervous syphilis and symmetrical cervical lipomatosis (*Sifilide nervosa e lipomatosi cervicale simmetrica*). Frigerio (A.), Riv. di patol. nerv. (Firenze), 1922, 27, 513-522.

The author reports a case of neuro-syphilis in which dystrophia adiposa developed immediately after the nervous and mental symptoms. On account of decreased sexual power, somnolence, feeling of cold and asthenia the author believes that the syphilitic infection which caused the nervous symptoms may have produced a lesion of either the hypophysis or the hypothalamic region.—G. V.

HYPOPHYSEAL cachexia (Beitrag zum Bilde der hypophysären Kachexie). Knoll (W.), Wien. Arch. f. inn. Med., 1922, 4, 555-572

Hypophyseal cachexia, in Germany also called "Simmonds' disease," is rather rare. In this article a case is described and the literature is reviewed. The author concludes that it is a well defined disease. The cardinal symptoms are precocious senility, loss of body hair, loss of sexual functions, and dullness. The symptoms generally develop long after the lesion (embolus of an arteriola propria of the hypophysis) which caused the disease takes place. Cases have been reported in which this embolus was caused by tuberculosis, syphilitic or septic infections, the last class containing cases of puerperal fever almost entirely. This probably explains why the disease is much more frequent in women than in men. It is highly probable, though the reported cases are not yet absolutely convincing, that pneumonic infections may also give rise to Simmonds' disease. The disease is seen only in adults. For diagnosis the Abderhalden test with an antigen from the pars anterior of the pituitary is recommended by the author. "Forme fruste" of Simmonds' disease is amenable to treatment, though diagnosis may be extremely difficult, especially when other diseases complicate the clinical picture. Tuberculosis of the hypophysis is suggested as another cause of the disease. The author thinks that this disorder may often pass unnoticed, hence may not be so rare as is generally believed.—J. K.

So-called **HYPOPHYSEAL** infantilism with tumor of the third ventricle and intact **HYPOPHYSIS** (*Infantilisme dit hypophysaire par tumeur du troisième ventricule. Intégrité de l'hypophyse*). Lereboullet (P.), Mouzon (J.) & Cathala (J.), *Rev. neurol. (Par.)*, 1921, 28, 154-159.

Report of the case of a young man who stopped growing at 13 years of age; at 17 years he presented true signs of intracranial tumor, with hemianopsia among other ocular disturbances; at 23 years he had the appearance of a boy of 14 with scarcely perceptible obesity and complete genital atrophy. Four years later he was fatter and seemed to show a Babinski-Frölich's adiposogenital syndrome. He grew 7 centimeters during this period. He became completely blind in one eye and had hemianopsia in the other. The sella turcica was normal, but calcifications of the clinoidal region suggested the presence of a neoplasm. The patient died 13 years after the beginning of his troubles and at autopsy the case seemed relatively typical. A tumor was found, projecting in the interpeduncular space of the brain, limited by a calcareous layer on the chiasm and compressing the pituitary stalk. The tumor occupied the entire middle region from the inferior wall of the lateral uninjured ventricles to the base of the brain. This tumor was histologically a papillary epithelium of the third ventricle. The hypophysis, more flattened than normal, weighed 44 centigrams, but presented no histological lesion; the other endocrine glands were normal. This case may be compared with those of Vigouroux and Delmos, and

of Marañon and Pintos, thus throwing light upon the problem of the respective rôles of the hypophysis and of the floor of the third ventricle in the genesis of adiposogenitalis. Although the hypophysis was intact, the infundibular stalk was compressed by the tumor. The authors discuss the two possible interpretations, hypophyseal and tubero-infundibular, but come to no formal conclusion.

—Author's Abst.

DIABETES INSIPIDUS of HYPOPHYSEAL origin (Manifestacione soculares en un enfermo con diabetes insipida de origen hipofisario). Marin (A.), Arch. de oftal. (Barcelona), 1921, 250; 533-542.

Owing to its anatomical situation, when there is enlargement of the hypophysis, the optic chiasma is compressed in such a way that completely distinct affections such as acromegaly and Frölich's syndrome present identical or similar visual lesions. In the one case the author encountered visual acuteness, dyschromatopsia, papillary atrophy in both eyes and bitemporal hemianopsia. Opthotherapy (injections of pituitary) notably improved the acuteness of chromatic vision and slightly the general visual, but the deeper lesions remained in the same condition.—E. B.

(HYPOPHYSIS) On the maintenance of "obstetric anesthesia" by means of infundibulin and chloroform. Martin (A. F.), Brit. M. J. (Lond.), 1922, ii, 672-674.

Light chloroform anesthesia commencing with the onset of labor pains, plus repeated small doses of infundibulin, are recommended to maintain an active uterine reflex. When cervical relaxation is practically complete, 0.5 cc. of infundibulin is injected intramuscularly and as the pains increase intermittent chloroform anesthesia is given. After about one-half hour the vigor of the pains abates and the infundibulin is repeated. Six doses in 3 hours is the greatest number cited. The average is 3 doses in 1½ hours. This treatment does not increase the number of postpartem hemorrhages and no toxic effects have been observed, although a few of the patients have shown increased pulse rates toward the end of and after labor. Thirty-two cases were studied.—R. E. K.

HYPOPHYSEAL cachexia, pituitary coma and pituitary lethargy. Mieremet (C. W. G.), Geneesk. Bl. u. Klin. en Lab. v. d. prakt. (Haarlem), 1922, 23, 235-268.

Complete or incomplete destruction of the anterior lobe of the hypophysis may cause hypophyseal cachexia, as described by Simmonds, but the same anatomical lesion may also cause coma or lethargy. In these cases organotherapy with hypophysis is sometimes effective. The cachexia as well as the coma and pituitary lethargy may have different causes, such as emboli, tuberculosis,

syphilis, malignant or benign tumors and inflammations of unknown origin. The author describes a case which is especially remarkable because the patient was a man, whereas nearly all cases of this kind are in women. He points out that pathologists should observe at autopsy the hypophysis of subjects who die of encephalitic lethargy.

—J. K.

(GONADS) Visual troubles in Frölich's disease (*Trastornos visuales en la enfermedad de Frölich*). Poyales, Arch. de oftal. (Barcelona), 1921, 246-302; 307.

Ophthalmoscopy often permits diagnosis in advance of hypophyseal manifestations. The enlargement of the gland determines a series of visual troubles that may be classified in two groups, namely, functional and organic. Among the functional disturbances the most important are bitemporal hemianopsia, augmentation of the blind spot and the existence of scotomata in the stereoscopic vision. Those included in the organic group are optical neuritis, optic hemiatrophia, post neuritica and exophthalmos in both eyes.—E. B.

The influence of x-rays on the HYPOPHYSIS (*Experimentelles zur Röntgenbestrahlung der Hypophyse*). Rahm (H.), Beitr. z. klin. Chir. (Tübing.), 1922, 126, 642-657.

When the hypophysis of rabbits is exposed to a stimulating dose of x-rays the rapidity of growth may be increased; in man the same experiment may be followed by temporary diabetes insipidus. Large concentrated doses of x-rays on the hypophysis diminishes or completely arrests growth. It is impossible to decide whether these experiments are important in human pathology.—J. K.

The influence of PITUITARY extracts on the absorption of water from the small intestine. II. Action of pituitary extracts when introduced into the alimentary canal. Rees (M. H.), Am. J. Physiol. (Balt.), 1922, 63, 146-150.

It has been shown that subcutaneous injections of pituitary extracts delay the absorption of water. In this paper it is shown that the same is true when pituitary extracts are introduced directly into the lumen of the small intestine in dogs and cats.—T. C. B.

The Golgi apparatus in the glandular cells of the HYPOPHYSIS. Functional polarity and the secretory cycle (*L'appareil de Golgi dans les cellules glandulaires de l'hypophyse. Polarité fonctionnelle et cycle sécrétoire*). Reiss (P.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 255-256.

Combining the Cajal technique with those methods which demonstrate the commoner cytoplasmic and nuclear structures, the author has studied the hypophysis in the calf, dog and cat. Best

Histological. Other conditions than gestation give rise to erythropoietic centers in the hypophysis.—T. C. B.

Erythropoietic centers in the **HYPOPHYSIS** of the pregnant guinea-pig (*Foyers d'érythropoïèse dans l'hypophyse de Cobaye gravide* Watrin (J.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 558-559).

Histological.—T. C. B.

Cachexia **HYPOPHYSEOPRIVA**. Zondek (H.), *Klin. Wchnsch. (Berl.)*, 1922, 1, 1385; *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1297.

Report of a woman of 42 who had ceased menstruating when she was 34. She had gradually become thinner and finally severe cachexia developed. She now weighs 30 kg. The blood pressure is low; metabolism is much retarded; the thyroid cannot be felt; when extra doses of water or salt are ingested they are largely retained in the organism.—J. K.

The output of sugar from the **LIVER** as affected by **Cu** and minimal **EPINEPHRIN**. Snyder (C. D.), Martin (L. E.) & Levin (M.), *Am. J. Physiol. (Balt.)*, 1922, 62, 442-458.

The reverse action of minimal amounts of epinephrin has been demonstrated for the portal-venous system of the terrapin's liver. The present paper discusses how the output of sugar from the liver under similar conditions is affected. The same method was used as in the other experiments. The output of reducing substances per unit of time in the venous outflow is greater for the solution of lower pH, and less for the solution of higher pH. When minimal effective amounts of adrenalin are added to the perfusion fluid the minute-volume flow is less for solutions of higher pH, and greater for solutions of lower pH. This is due to the effects of adrenalin on vascular caliber and hence on intensity of irrigation rather than to a specific "epinephrin reversal."—T. C. B.

Evolution of the endocrine islands of the **PANCREAS** (*L'évolution des îlots endocrines du pancreas*). Aron (M.), *Arch. d'anat., d'histol. et d'embryol. (Strassb.)*, 1922, 1, 71-107.

The pancreatic islets should be distinguished into those of Laguesse and of Langerhans. In the embryonic pancreas the former appear first, and are regarded as the homologue of, and have a similar origin as, hepatic tissue; their physiological significance is still obscure. The islets of Langerhans appear later; their appearance is concomitant with the establishment of the glycogenic function of the liver. Morphological difference (staining reactions, etc.) are described between the 2 sets of islets in the 4 animals investigated (sheep, pig, guinea pig, and man).—Physiol. Abst., 7, 448.

The relations between acids and bases and TETANY with special observations on the rôle of the phosphoric acid ion (*Über die Beziehungen von Säure und Alkali zur Tetanie mit besonderer Berücksichtigung des Phosphorsäureions*). Elias (H.), Wien klin. Wchnschr., 1922, 35, 784-786.

Many German authors think that disturbed acid-base regulation is the most important cause of tetany, but Elias confirmed the results of others, especially American investigators, who state that this factor is not important. The question of the treatment of tetany with acids or alkalies is not yet settled. Four facts, however, seem to have been established: (1) large quantities of acids increase in man and animal the irritability of the nerves; (2) small doses decrease this irritability; (3) alkalies increase the irritability; and (4) the PO_4 ion increases nervous irritability in normal and in tetanic subjects.—J. K.

The response of the submaxillary glands of the albino rat to **THYRO-PARATHYROIDECTOMY** and to **PARATHYROIDECTOMY**. Hammett (F. S.), Am. J. Anat. (Phila.), 1922, 31, 103-107.

Using the "gentled" stock from the Wistar colony of albino rats, Hammett found that removal of the parathyroid glands results in a marked increase in the size of the submaxillary glands. The same result does not follow thyro-parathyroidectomy. Hence the enlargement cannot be attributed to any local irritation produced by the operative procedure. As a possible explanation it is suggested that the hypertrophy or hyperplasia is a response to an increased functional activity induced by the increased neural irritability resulting from the removal of the parathyroids.—W. J. A.

Three total **THYRO-PARATHYROIDECTOMIES** in the dog, with special observations concerning respiratory perturbations (*Tres tiro-paratiroidectomias totales en el perro, con observacion especial acerca de las perturbaciones respiratorias*). Ocaranza (F.), & Macedo (J. P.), Rev. mex. de biol. (Mexico, D. F.), 1922, 2, 268-286.

In general the classic picture of thyro-parathyroid deficiency was noted. It is commonly stated, however, that the temperature falls immediately after this operation and that within 24 hours it notably ascends. In the first of the experiments reported hypertonia appeared 48 hours after the operation. In the second hypertonia appeared a few hours after the operation and, the next day, hypothermia. In the third experiment there was no hypertonia. The authors believe that vomiting, diarrhea and sialorrhea are not constant manifestations, but that tachycardia, hypertension, dilation of the pupils and congestion of the conjunctiva are characteristic. The respiratory disturbances in the three experiments were very similar. The primary phenomena consisted of polypnea, augmentation

of the amplitude of respiration, arrhythmia, alternating respiration, brusque inspiration and prolonged expiration, this latter at times consisting of two convulsive efforts, the whole picture resembling that following double vagotomy. The tachycardia, with systolic augmentation and hypertension, the dilation of the pupils and the irritation of the conjunctiva, led the authors to think that the thyro-parathyroidectomized subject is in a state of sympatheticotonus.

—W. H.

(PARATHYROID) Relation between the chemical processes in the body and TETANY (Ueber die Beziehungen des Chemismus des Organismus zur Tetanie). Orgler, Deutsche med. Wchnschr (Berl.), 1922, 48, 1008-1010; 1037-1038.

A review of the literature on chemical studies of the blood, urine and organs in tetany. Not only are calcium and phosphorus metabolisms of tetany but the excretion of comparatively large doses of acetone in the presence of guanidine in the urine and the large quantity of this substance in the stools must be explained. Most publications of small value because they deal with only a small number of cases. NEPHRIN. Since because in the estimation of calcium an exact method is not used, such as Wright's or Bang's method. The reverse action is better. All authors do not agree whether the concentration of the blood is normal in tetany. Although tetany is present in guanidine tetany and tetany of infants are not under similar conditions improve when large quantities of calcium are administered. The low calcium content of the blood probably causes the increased irritability.—J. K.

Influence of endocrine gland substance on morphogeny. Feeding tadpoles with PARATHYROIDS (Versuche über den Einfluss endokriner Drüsensubstanzen auf die Morphogenie). Schulze (W.), Arch. f. Entwicklungsmechn, d. Organ. (Berl.), 1921, 48, 489-504.

The report deals with the results of feeding fresh bovine parathyroids, parathyroid extract (Freund-Redlich) and accessory thyroid (parathyroid?) tablets (Freund-Redlich), alone or in connection with thyroid, testicular and ovarian tissue, to 150 *Rana fusca* and 8 *Bombinator pachypus* larvae in different stages of development. Body measurements were made under light anaesthesia. The size of the thyroid, thymus, pineal gland and hypophysis was determined in some cases. Many animals were fixed and sectioned serially for histological study. The author found that fresh parathyroid produced (after an initial nonspecific acceleration in growth) no influence on development or metamorphosis. The parathyroid tablets accelerated metamorphosis but decreased the rate of growth, giving results similar to those produced by feeding fresh thyroid gland. Twenty-six references are given.—A. T. R.

(PARATHYROID) The influence of meat diet on experimental TETANY. Sinelnikov (E. I.), Russ. J. Physiol., 1922, 4, 18-33.

Raw meat diet has no effect on thyroidectomized dogs, but increases the symptoms of tetany in parathyroidectomized dogs. The galvanic action in a normal dog was C.C.C.-2.0 milliamps, A.C.C.-2.8, A.O.C.-3.0, C.O.C.-5.6; after parathyroidectomy it changed to 1.4, 2.2, 2.8 and 2.8, and each time about 6½ hours after administration of 400 gm. of raw meat it was 0.4, 0.9, 0.9 and 1.4, respectively; c-tetanus was produced in the latter case with 2.0 m.a. and a-tetanus with 4.6 m.a. The active substance is soluble in water; boiled meat has no effect. Liebig's extract (4.5 gr. per kilo internally) causes severe convulsions. Guanidine, methylguanidine, carnitine and ablitine were found to be the active principles.

—Physiol. Abst., 7, 445-446.

(PARATHYROID) Post-operative TETANY and pregnancy (Post-operative tetanie en zwangerschap). Stenvers (H. W.), Nederl. Tijdschr. v. Geneesk (Haarlem), 1922, 66 (II), 1049-1054.

Double strumectomy was performed on a woman in two operations. Immediately after the second operation she had a very severe attack of tetany. Large doses of fresh parathyroid were followed by good results. Transplantation had a very good effect, though spasms were still observed, especially during menstruation. Pregnancy five years later had a splendid influence, although some symptoms reappeared during the period of lactation. The author believes that this case proves that the general opinion as to the danger of tetany in pregnancy is unfounded.—J. K.

Tumors of the PARATHYROIDES and their relation to osteomalacic diseases of bone (Über Epithelkörperchentumoren und ihre Beziehungen zu den osteomalacische Knochenerkrankungen). Strauch (B.), Frankfurt Ztschr. f. Path. (Weisb.), 1922, 28.

The author discusses the possible relation to the incretory glands of diseases in which calcium metabolism is disturbed, such as rickets, osteoporosis, puerperal, senile and hunger osteomalacia and osteitis fibrosa. Some of the relations of the gonads, the thyroid, thymus, suprarenals, hypophysis and parathyroids to the osteomalacic diseases are discussed. He reports a case of puerperal osteomalacia in a woman aged 27 years which terminated fatally three months after delivery. In addition to the generalized bone softening, tumor 4.8x3.2x3.5 cm., presumably involving the left internal parathyroid, was found. No other parathyroids were seen. In addition to several cystic spaces filled with clear fluid the parenchyma was composed of two types of cells, the principal, or basophilic cells, and groups of acidophilic cells. The cells were arranged in strands and an occasional follicle formation, i. e., not

essentially different from normal. Strauch was unable to make out any significant changes in the other glands of internal secretion. He refers to a number of similar cases with parathyroid tumor and bone softening reported in the literature and also to cases with parathyroid enlargement without bone changes. It is also known that marked softening of the bones may occur without demonstrable changes in the parathyroids. On this account the author concludes that tumors of the parathyroid give very little information regarding the causes of bone softening. They, however, add further evidence to the relationship between the parathyroid function and calcium metabolism.—S. S. (D. M.)

Tumors of the PINEAL gland (*Die Zirbel und ihre Tumoren in ihrem funktionellen Einfluss*). Askanazy (M.), Frankfurt Ztschr. f. Path. (Weisb.), 1921, 24, 58-78.

The author reviews some of the theories of the function of the pineal gland and summarizes the information concerning its function that has been obtained from a study of its tumors. He reviews 11 cases of tumor, 8 of which were certainly teratomata, one probably a teratoma, one a chorio-epithelioma and one a glioma. These groups when occurring in males before the age of puberty were usually associated with precocious sexual development. The evidence of anatomical, clinical and experimental work to date favors the conception that the pineal gland functions usefully throughout life.—H. L. J. (D. M.)

The extirpation of the PINEAL gland and its influence on the HYPOPHYSIS (*L'extirpation de la glande pinéale et son influence sur l'hypophyse*). Urechia (C. I.), & Grigoriu (C.), Compt. rend Soc. de biol. (Par.), 1922, 87, 815-816.

After removing the epiphysis from a great number of cocks the authors succeeded in maintaining two alive for 8 months. At first there was an involution of secondary sex-characters, but later development was rapid. Eight months after the extirpation of the pineal the animals were sacrificed. They appeared no different from the controls of the same generation. The weight of the testicles was the same as that of the controls, but microscopically there was a greater development of interstitial gland. The hypophysis was much larger in the animals that had been operated upon, with hypertrophy of the pars nervosa. Its structure indicated a hyperfunctional state.

—T. C. B.

The histology and physiology of the human PINEAL gland (*Zur Histologie und Physiologie der menschlichen Zirbeldrüse*). Walter (F. K.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl.), 1922, 74, 314-330.

Correction of Endocrinol., 1922, 6, 910.—A. T. R.

SECRETIN studies (*Etude sur la sécrétine*). Djenab (K.), *Ann. de méd. (Par.)*, 1922, **12**, 475-479.

Brief report of some work with rabbits which showed that secretin is partly destroyed by the liver, and that diet has an influence on the activity of the substance.—F. S. H.

Comparative studies of the activity of SECRETINS of the digestive tract (*Vergleichende Untersuchungen über die Wirkungsstärke der Secretine des Digestionstractus*). Haramaki (K.), *Biochem. Ztschr. (Berl.)*, 1922, **129**, 503-506.

All parts of the gastric mucosa produce secretin. Extracts from fundus, duodenum, rectum, colon and jejunum show secretin activity. The latter is a bit the weaker. Administration by mouth gives less reaction than does intravenous injection. Dogs were used in the experiments—F. S. H.

Influence of SECRETIN solutions on intestinal motility (*Ueber den Einfluss von Secretinlösungen auf die Darmmotilität*). Haramaki (K.), *Biochem. Ztschr. (Berl.)*, 1922, **129**, 128-133.

The injection of histamine and spinach secretin into the ear-vein of a rabbit so prepared that direct observation of intestinal movement could be made was followed by intestinal peristalsis.—F. S. H.

The effect of SPLENECTOMY on integration of muscular movements in the rat. Macht (D. I.) & Finesilver (E. M.), *Am. J. Physiol. (Balt.)*, 1922, **62**, 525-530.

Rats were trained to walk on a rope. It was found that extirpation of the spleen did not interfere with the coördination of the muscles or the running time of the animals. If anything, both were improved.—T. C. B.

The SPLEEN as an incretory organ (*La rate envisagée comme glande à sécrétion interne*). Stern (L.), *Rev. suisse de méd.*, 1922, No. 25 (June); abst., *Arch. méd. belge (Brux.)*, 1922, **75**, 816.

Stern, in collaboration with Rothlin, found in the spleen and in the blood of the splenic vein a substance, "liénine," that augmented both the tonus of the smooth muscle fibers and their sensitiveness to adenalin. Experiments were performed to demonstrate that, due to liénine deficiency, extirpation of the spleen caused the stimulating power of the blood on the vessel walls to diminish and the normal tonus of the smooth muscle fibers to change. Examination of the former did not give conclusive results, the factor being too variable even in the same subject. Alteration of the tonus of the smooth muscle fibers was studied indirectly by examination of the action of adrenin in animals before and after splenectomy. In the dog and

cat splenectomy did not modify the sensitiveness to adrenalin, but in the rabbit it took very large doses to give a pressor reaction equal to that previously obtained, although in the splenectomized animal the blood pressure remained as high as in the normal animal.

—R. G. H.

Status THYMICOLYMPHATICUS. Estill (R. J.), Proc. Kentucky State M. Ass., October 16-19, 1922.

A history of frequent severe colds with wheezing in the chest should make one suspect status lymphaticus, likewise the presence of enlarged tonsils with hyperplasia of the faucial and pharyngeal lymphatic tissue and enlarged lymph glands in infants under 2 years of age. It is probable that a complete examination of children under 2 years of age would show that status lymphaticus is more common than is believed to be the case. A roengen-ray examination of the chest should be made of every child giving a history of frequent colds or attacks of wheezing in the chest. Except in cases of sudden death in new-born infants and in neglected cases, the roentgen ray offers a very favorable prognosis in status lymphaticus.

—J. Am. M. Ass., 79, 1793.

Status THYMICOLYMPHATICUS in infancy. Kohlbry (C. O.), Proc. Minnesota State M. Ass., October 12-14, 1922.

Kohlbry's patients were infants, the ages varying from 1 to 9 months. None had had any earlier illness. They all died with the first infection. Evidence of infection of comparative mildness was present in every case—an upper respiratory affection described as a cold. These infections were not accompanied by any considerable amount of fever. The illnesses were of short duration, three children having been sick only three days, while the others had had a cold for from one to two weeks before, with none but the local symptoms. Evidences of a pathologic condition in the thymus were found in all. Three patients showed stridor, and two showed, in addition, a dyspnea which was probably cardiac in origin. There was a definite roentgenographic shadow, such as is generally considered to be due to an enlarged thymus, in the only two cases submitted to roentgen-ray examination. In one case, a thymic area of dullness was obtained on percussion. The postmortem examination showed that the thymus weighed 13 gm. or more, the largest weighing 27 gm. There were hemorrhages into the gland in four of the five cases. Lymphoid hyperplasia was found elsewhere in the body in all cases, and was most evident in the mesenteric glands and the mesenteric follicles of the intestines. Sudden death was conspicuous in all cases. This occurred practically without warning. Evidence of septic disease was not lacking, as is shown by hemorrhages into the lungs. Two cases showed large hearts, with symptoms of cardiac failure in addition.—J. Am. M. Ass., 79, 1792.

Serous-ferment perturbation and histological modifications of the principal digestive organs after **THYMECTOMY** (*Perturbamento siero fermentativo e modificazioni istologiche dei principali organi digestivi in seguito a timectomia*). Ruggeri (E.), *Folia med.* (Napoli), 1922, 8, 225-233; 275-280.

After total ablation of the thymus in the pigeon a few symptoms appear, as post-operative weakness, with later exaggerated appetite, and more fluid and acid excreta. The enzyme production was temporarily perturbed. The complement titre was diminished and thymectomized animals were easily infected. A histological study was made of some organs related to the digestive apparatus. Diminution of glycogen in the liver and changes in the mitochondria of the pancreas and duodenum were found.—G. C.

(**THYROID**) Pregnancy in a myxoedematous woman (*Grossesse chez une myxoedemateuse*). Audebert & Claverie, *Bull. Soc. d'obst. et de gynec. (Par.)*, 1921, 20, 79-80.

A case report illustrating the diminution of hypothyroid symptoms during pregnancy. The latter is associated with a hypertrophy of the thyroid, and almost always with an increased function. This explains the autotherapeutic effect exerted upon myxoedema by pregnancy.—E. N.

(**THYROID**) Myxedema and imbecility (*Myxoedème et imbécillité*). Ballif (L.), *Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy*, 1921, 3, 1-2 (September).

Presentation of a case. The important factor in this case is the fact that patient had a sister with goiter. Attention is drawn to diversity of manifestations of thyroid disorders.—F. S. H.

Action of iodine and of iodides upon the **THYROID** of healthy and tuberculous guinea pigs. Bezançon (F.) & de Jony (S.-I.), *Rev. tubercul.*, 1920, 1, 36-39; *Abst. Bact.*, 5, 165.

The thyroid gland of the normal guinea pig weighs 0.05 to 0.07 gm. KI or Gram's iodide causes the vesicles to distend and the epithelium to flatten out, but with an absence of interstitial hyperplasia; the reaction is more pronounced with subcutaneous injection than with mouth ingestion. With iodized water or oil there is a distinct and marked hyperplasia, increasing in weight to 0.36 gm. at times. The gland in a tuberculous pig resembles that of a tuberculous person. Iodine has no influence on the course of the disease. The gland tends to become normal, the epithelium being entirely normal. KI on the other hand causes an intense vascular congestion.

—Chem. Abst., 16, 3975.

THYROTOXICOSIS. Blackford (J. M.), *Surg., Gynec. & Obst. (Chicago)*, 1922, 34, 185-188 (February).

The treatment of exophthalmic goiter is essentially surgical. Early diagnosis is important. The mortality from removal in non-toxic or mildly toxic cases is almost zero in competent hands, and the net results are satisfactory. The cardiac reserve of the patient is nearly always good enough to withstand operation. The bulk of surgical mortality occurs in the badly toxic cases, not in cases of extreme cardiopathy.—E. N.

The THYROID problem (*Untersuchungen zur Schilddrüsenfrage*). Breitner (B.), *Wien. klin. Wchnschr.*, 1922, **35**, 969-971.

General discussion.—J. K.

(THYROID) Problems of Graves' disease (*Problemstellung beim morbus Basedowi*). Breitner (B.), *Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena)*, 1922, **35**, 637-650.

There is a very close relation between the sexual organs and the thyroid. Physiological hyperfunction of one causes physiological hyperfunction of the other. Graves' disease is more frequent in women, due to menstruation, pregnancy and childbirth. This may account for the beginning of Graves' disease at the time of first menstruation. In man, too, it is not unusual to find sexual disorders as important factors in the pathogenesis of Graves' disease. Generally hyperfunction of the sexual organs is the primary cause; primary hyperfunction of the thyroid is rare. The familiar form of Graves' disease, however, may be due to anatomical variations. Diseases giving rise to fever may cause increased absorption of the thyroid hormone, thus causing hyperthyroidism. The clinical picture depends upon the intensity of the symptoms, originating in the thyroid. Classical Graves' disease is caused by a combination of increased or decreased activity of the complete endocrine system. The theory that dysfunction of the thyroid causes Graves' disease is not accepted by Breitner. He remarks that it is impossible to prove the existence of this dysfunction. The author does not believe that the problems concerning exophthalmic goiter have been solved, but hopes by his theories to reduce the confusion now existing in endocrine literature.—J. K.

Studies on the condition of activity in endocrine glands. IX. Further evidence of nervous control of THYROID secretion. Cannon (W. B.) & Smith (P. E.), *Am. J. Physiol. (Balt.)*, 1922, **60**, 476-495.

Cats under light ether anesthesia were used. Massage of the thyroid for 2 or 3 minutes causes increased rate of the denervated heart, reaching a maximum in from 30 to 60 minutes. Augmentation occurs in the absence of the adrenals. If the thyroid has been previously removed, stimulation of the cervical sympathetic trunk as it leaves the stellate ganglion also augments the denervated heart.

Sensory stimulation and asphyxia induce a brief augmentation after removal of the thyroids, due to adrenal and hepatic discharge. If the cardiac fibers from the stellate ganglion, and also the vagi are cut, stimulation of an afferent nerve (sciatic or brachial) will cause a primary increase due to adrenal secretion, followed by a more slowly developing thyroid effect. The same is true of asphyxia under similar conditions. Compared with vascular reactions as a test of thyroid activity this has the advantage of not requiring destruction of the upper portion of the central nervous system. In an addendum it is stated that these experiments were repeated in March and April with negative results, due to seasonal variations in iodine content of the thyroid.—T. C. B.

(**THYROID**) *Lues hereditaria tardia: Endocrinopatías.* Castex (M. R.) & Waldorp (C.), *Prensa méd. argentina* (Buenos Aires), 1920, 7, June 10.

Graves' disease is produced in a large number of cases by late hereditary lues. Familial cases are seen in syphilitic families.

—B. A. H.

Unilateral tumefaction of the THYROID, breast and testicle in a soldier with war traumatic neurosis (*Tumefazione unilaterale della tiroide, della mammella e del testicolo in un soldato con nevrosi traumatica di guerra*). Chimisso (L.), *Folia med.* (Napoli), 1922, 8, 481-496.

An interesting clinical case in which the syndrome consisted in paralysis and anesthesia of the right arm, lagophthalmus, exophthalmus, and mydriasis on the right, swelling of half the thyroid, testicle and breast of the same side, and analgesia of the testicle. The etiology consists in a traumatic neurosis from war shock, which affected only the right sympathetic.—G. C.

THYROID gland and tuberculosis (*Corps thyroïde et tuberculose*). Coulaud (E.), *Thèse de Par.*, 1922; abst., *Presse méd.* (Par.), 1922, 30, 992.

There has been a tendency of recent years to consider that thyroid deficiency leads to predisposition to tuberculosis. After having studied the function of the thyroid in connection with the immunity phenomena, the author concluded that there is no ground for this hypothesis. He tubercularized hypothyroid rabbits, but these animals lived even longer than the controls. Histologically the thyroid in the tuberculous subject appeared to function normally. Clinical observations confirm this theory; patients with simple goiter, with Graves' disease, and with myxedema are tuberculous only exceptionally. But in women times of physiological hyperthyroidism coincide with periods of lowered resistance; tuberculosis is most active during menstruation, pregnancy and the menopause. Coulaud cites some

curious instances in which tuberculosis seemed to become manifest under the influence of thyroid opotherapy. Ovarian opotherapy, which is often used to moderate thyroid function, seems capable, in a large number of cases, of contributing to the reestablishment of allergy.—R. G. H.

Action of x-rays on the **THYROID** of the adult rabbit (*Action des rayons X sur le corps thyroïde du lapin adulte*). Coulaud (E.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1014-1016.

Histological description of the thyroid after irradiation of various intensities and at various times after irradiation has been discontinued.—T. C. B.

(**THYROID**) Clinical types of goiter and their management. Elliott (C. A.), *Med. Clin. N. Am. (Phila.)*, 1922, **5**, 1623 (May).

This author says: "We have not observed the definite and lasting results which would stamp these agents as all sufficient in the treatment of hyperthyroidism," but it is stated that perhaps these agents have not been perfectly applied. "In general it must be admitted that radium and x-ray may be sufficient in any given case and that they are useful in reducing hyperthyroidism preliminary to operative interference." In selected cases of toxic goiter radium or x-rays may be indicated and in exophthalmic goiter they may be advisable preliminary to a subtotal thyroidectomy.

—J. Radiol., **3**, 509.

The quantity of iodine in **THYROID** extracts (*Sur le dosage de l'iode dans les extraits thyroïdiens*). Fabre (R.) & Penau (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1026-1028.

(**THYROID**) Methods and technic of goiter operations (*Ueber Methodik und Technik der Kropfoperation*). Flörcken (H.), *Beitr. z. klin. Chir. (Tübing.)*, 1922, **127**, 85-97.

See *Endocrin.*, **6**, 731.

Iodine contents of the **THYROID** of the Japanese. Fukushima (T.), *J. Jap. Soc. Int. Med.*, 1921, **9**, No. 5; *Jap. Med. World*, 1922, **2**, 45.

The average total weight of the thyroid of the Japanese is $\frac{1}{2}$ that of the European. The distribution of I in the bilateral lobes occurred evenly; the average was 0.81 mg. in the left and 0.811 mg. in the right, per 1.0 gm. fresh glands. The Japanese thyroids contained, comparatively, remarkably larger amounts of I, probably because of the rich fish diet.—*Chem. Abst.*, **16**, 3951.

Physiology of the frog's **THYROID** (*Contributo allo studio della fisiologia della tiroide della rana*). Gayda (T.), *Arch. di fisiol. (Firenze)*, 1922, **20**, 209-224.

Thyroid extirpation and administration experiments on frogs (18 in all, including controls) were performed. There was no appreciable morphological or functional difference in the results following thyroid extirpation in winter and summer frogs. As an immediate consequence of the operation the heat production gradually diminished to the time of death. This was not very considerable in the winter frog (14 to 28%); in the summer animal it was more marked (31 to 42%). In every case the heat production value changed in one way only until the death of the animal, some months after the extirpation. Ingestion of sheep's thyroid into the normal or thyroidectomized frog never produced any phenomenon resembling hyperthyroidism. The heat production either did not vary, or showed a slight and transitory increase of not more than 10%, and lasted not more than 2 or 3 days. Feeding by mouth either sheep's thyroid or flesh produced no marked differences from normal. It is concluded that the frog's thyroid is not of the same importance in heat regulation as that of homothermal animals, and in the frog is of more importance in the developing animal than in the adult

—A. T. C

Studies of the THYROID apparatus. VIII. On the alleged exogenous source of the poisons giving rise to tetania parathyreopriva. Hammett (F. S.), *Am. J. Physiol. (Balt.)*, 1922, 63, 151-154

Two groups of 24 white rats each were put on a diet, one group exclusively meat, the other exclusively lettuce. After 4 days they were all parathyroidectomized. Of those on a meat diet, 37.5% died in 48 hours; of those on a lettuce diet, 58.4% died in 48 hours, all of acute tetany. The rats with a low exogenous metabolism of protein had the greatest mortality, and the author thinks this disproves the conclusion of Luckhardt and Rosenbloom that "the" source of the poison responsible for tetany is of exogenous origin; it is only 'a' source.—T. C. B.

(THYROID) A possible factor in the increasing incidence of goiter. Hayhurst (E. R.), *Science (N. Y.)*, n s 54, 131

The suggestion is made that the increasing incidence of goiter is due to the use of purified NaCl as a condiment instead of sea salt as in former times.—F. A. H.

(THYROID) Alteration of metabolism after chronic administration of morphine (Ueber Veränderungen des Stoffwechsels nach chronischer Morphinzufuhr). Hildebrand (F.), *Archiv. f. exper. Path. u. Pharmacol. (Leipz.)*, 1922, 92, 68-95.

From the results of respiration experiments obtained on four rats (by means of Rohde apparatus) the author concludes that there is an analogy between the effects of thyroidectomy and the chronic administration of morphine. In both cases there was a decrease of

the oxygen consumption for 3-4 weeks and an increase of the respiratory quotient (perhaps due to an increased combustion of carbohydrates). In both cases the administration of thyraden was followed by a rise of the low basal metabolism and by a decrease of the respiratory quotient. The thyroidectomized and the chronically morphinized rats showed a diminished sensitiveness to lack of oxygen. The sensibility for morphine increased after administration of thyroid substance and decreased after thyroidectomy.

—R. W.—A. B.

(THYROID) Experimental study of the pathogenesis of exophthalmos. Idzumi (G.), Tokyo Iji-Shinshi, 1922, No. 2278 (May); abst., Jap. Med. World, 1922, 2, 296.

Idzumi discovered that functional derangement of the epithelial body results in swelling of the thyroid. He extirpated the epithelial bodies of a guinea pig and fed it with calcium and phosphorus. The animal thus fed showed a swollen thyroid. Characteristics of the teeth and microscopical findings of the thyroid both showed manifestations similar to those in human cases of exophthalmos.—R. G. H.

(THYROID, PARATHYROID, THYMUS) Branchial derivatives in turtles. Johnson (C. E.), J. Morphol. (Phila.), 1922, 36, 299-329.

The development of the branchial derivatives was studied in turtles of the genera *Chelydra*, *Chrysemys*, and *Trionyx*. The results are of interest principally to the embryologist.—W. J. A.

The THYROID gland and sensibility of tuberculous animals to tuberculin (*Glande thyroïde et sensibilité des animaux tuberculeux envers la tuberculine*). Kepinow (L.) & Metalnikow (S.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 210-213.

Having previously studied the rôle of the thyroid in serum anaphylaxis, the present paper deals with an allied phenomenon—the reaction of tuberculous animals to tuberculin by a rise in temperature. The thyroid was removed from 4 guinea pigs, and 4 others were kept intact as controls. All were inoculated subcutaneously with a virulent culture of tubercle bacilli 8 days after the operation. A month later they were injected subcutaneously with tuberculin, some lethal, others not. The controls reacted by an elevation of temperature, while the thyroidectomized animals showed no appreciable rise. Those receiving a lethal dose of tuberculin, whether experimental or control, died. It would seem, then, that the rise of temperature, classed among the facts of anaphylaxis, is bound up with the thyroid function, while the purely toxic character of the tuberculin is not. In another series of animals the effort was made to confer a passive thermic sensibility by injecting the serum of tuberculous guinea pigs, thyroidectomized and non-thyroidectomized, into normal guinea pigs. All the non-thyroidec-

tomized animals reacted promptly, while the thyroidectomized did not respond. None of them died. It is assumed that only the thermic action is transmitted passively. The serum of thyroidectomized animals transmits neither the thermic sensibility nor the toxic effects.—T. C. B.

(THYROID) Treatment of goiter with parenchymatous injections (Ueber die Behandlung des Kropfes mit parenchymatösen Einsprinkungen). Krebs (G.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 898.

The author has injected about 1000 goiters with tincture of iodine. Only in vascular (especially) or cystic goiters were results obtained. To avoid thrombosis it is necessary to aspirate before injecting. If blood runs into the syringe the needle must be removed and the injection must be repeated in another part of the goiter. Ordinarily 5 to 8 injections are enough, but 20 may be necessary before good results are obtained.—J. K.

(THYROID) Atrophy of terminal phalanges in a rheumatic and sclerodermic patient with goiter, dying of tuberculosis (Atrophie des phalanges chez une goitreuse rhumatisante et sclérodermique, morte tuberculeuse). Laignel-Lavastine & Coulaud (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1526-1530.

(THYROID) Causes of death in goiter (Über die Bedingungen des Kropftodes). Lang (F. J.), Klin. Wchnschr. (Berl.), 1922, 1, 2461-2464.

A discussion of the dangers caused by toxic and non-toxic goiters and the different ways in which they may be responsible for sudden death.—J. K.

(THYROID) Influence of the parenteral administration of protein on gaseous metabolism (Ueber den Einfluss der parenteralen Eiweisszufuhr auf den Gassstoffwechsel). Leimdörfer (A.), Biochem. Ztschr. (Berl.), 1922, 133, 409-416.

These studies show that parenterally administered protein produces an increase in the oxidative processes which is accompanied by a rise in temperature. If the latter does not occur there is no change in gaseous metabolism. A discussion of the rôle of the thyroid and chemical heat regulation is given.—F. S. H.

Mental anorexia and the THYROID. Lévi (L.), Encéphale (Par.), 1922, 17, 507-516 (October).

Lévi reports some cases of mental anorexia in which thyroid treatment restored conditions to normal. The appetite returned and the three women gained in weight. Analysis of the cases shows absence of appetite from thyroid insufficiency. On this had

become superposed a mental condition aggravating the anorexia and perpetuating it.—J. Am. M. Ass., 79, 1961.

The red sign of the THYROID (*Sur la signe de la tache rouge thyroïdienne*). Marañón (G.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 1635-1641.

(THYROID) Intravenous chemical treatment of Graves' disease and goiter (*Eine intravenöse Chemotherapie der Basedowschen Krankheit und des Kropfes*). Mendel (F.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 896-897.

The administration of very small doses of iodine in Graves' disease, as recommended recently by some German authors, is not a new therapy. More than 10 years ago the author described a treatment in which NaI and atoxyl were given together. Every 2 days, and in light cases twice a week, 2 cc. of the following solution is injected: atoxyl, 1 gm.; NaI, 8 gm.; water, 40 cc. This combination can be bought in ampules and is called "jodarsyl." In simple goiters good results are also seen, although improvement is not so rapid as in Graves' disease.—J. K.

(THYROID) Development of goiter in children (*Die Entwicklung des Kropfes bei Kindern*). Messerli (F. M.), Rev. méd. de la Suisse Rom. (Genève), 1922, 42, 176; abst., Monatschr. f. Kinderh. (Leipz.), 1922, 23, 555.

From the standpoint of prophylaxis it is important to determine the age of the incidence of goiter. The author's studies on school children in a goitrous town showed that the goiter preceded their enrollment in school, hence prophylaxis should have been instituted previous to this time.—R. G. H.

HYPERTHYROIDISM. Murray (G. R.), Brit. M. J., 1922, 1, 905-908 (June 10).

A general article. Murray feels that surgery is indicated in cases which show pressure symptoms or evidence of rapidly advancing toxic myocarditis. In any case he believes that medical treatment should have a full trial for six months before surgery is considered.

—F. C. P.

Contribution to the morphologic study of the THYROID gland in Emys europaea. Naccarati (S.), J. Morphol. (Phila.), 1922, 36, 279-297.

A detailed study of the macroscopic anatomy, circulation, innervation and histology of the thyroid in two turtles, *Emys europaea* and *Testudo graeca*. The steps in the technique of Galeotti's staining method, which the author highly recommends, are detailed. There are two colored plates.—W. J. A.

(THYROID) Experimental studies on the so-called Kocher's blood features in exophthalmic goiter. Ohhara (H.), Nisshin Igaku, 1922, 11, No. 8 (April); cit., Jap. Med. World, 2, 300.

The sensitizing action of THYROID extract for adrenaline. Ono (S.), Jap. Med. World, 1922, 2, 157-160.

Using isolated organs, Ono found that an active principle of thyroid extract sensitizes the heart of the toad and the blood vessels of the cow for the action of adrenaline.—Chem Abst., 16, 3976.

Iron in the blood of THYROIDECTOMIZED animals (Sur la teneur en fer du sang des animaux euthyroïdes). Parhon (M.), Endocrin. e patol. costituz. (Roma), 1922, 1, 39.

In 6 sheep, thyroidectomized at the age of 6 weeks, the author found a diminution of iron in the blood, thus causing retardation of internal oxidation.—B. A. H.

Differential diagnosis of diseases of the THYROID gland. Phillips (J.), Canad. M. Ass. J. (Montreal), 1922, 12, 318-327.

Anaphylaxis and THYROID (Anafilassi e tiroide). Pistocchi (G.) Pathologica (Genova), 1922, 14, 717-718 (November).

Lanzenberg and Képinow's studies on the effect of partial thyroidectomy in reduction or prevention of anaphylactic crises agree with the previous publication of the author (1920). Képinow states that since in the transmission of passive anaphylaxis thyroidectomy is indispensable in the transmitting animal, the thyroid must elaborate the substances determining the shock. The author is inclined to believe, however, that the thyroid has an indirect value, that through thyroidectomy the whole organism changes and may become unable to prepare the substances necessary to anaphylaxis.
—G. V.

(THYROID) New medical treatment of goiter (Nouveau traitement médical du goître). Regnault, Soc. de méd. de Par., 1922, Nov. 10; abst., Presse méd. (Par.), 1922, 30, 1011.

The author gave 30 cgm. of thyroid extract and 3 mg. of parathyroid extract 3 times in 24 hours. This treatment was kept up for 3 weeks, followed by 8 days of rest. Good results were obtained in simple goiter, some cases of exophthalmic goiter and in thyroid insufficiency.—R. G. H.

Treatment of goiter by THYROID and PARATHYROID extracts (Traitement du goître par les extraits thyroïdes et parathyroïdes associés). Regnault (F.), Soc. de pathol. comparée, 1922, July 11; abst., Presse méd. (Par.), 1922, 30, 652.

Regnault, led to the use of this treatment by considerations of comparative anatomy, obtained some results which should encourage

investigators to attempt verification. After being assured of the condition of the circulatory system of the patient he prescribed 10 centigram pills of thyroid extract and 1 mg. wafers of parathyroid. The author advocates the administration of 1 pill and, three minutes later, 1 wafer before a meal (always watching the heart closely) for three or four days; then 2 pills and 2 wafers morning and evening, and, finally, 3 pills and 3 wafers, with a rest of 8 days every 3 weeks.—R. G. H.

(THYROID) The surgical treatment of exophthalmic goiter. Romanis (W. H. C.), *Lancet* (Lond.), 1922, ii, 471-475.

Only those patients are included in this article who showed rapid and definite cardiac changes, eye changes and typical findings on microscopic examination. Operative mortality is usually due to acute thyroid intoxication and occurs in the first 48 hours, the symptoms being a rapidly increasing pulse, fever, restlessness, delirium and acetonuria. Under local anesthetic this seems to be less—in the last group of 250 operations the mortality was 2.4%. In mild cases a period of observation may result in complete disappearance of the symptoms; more often surgical measures must be resorted to. In patients with maniacal, delusional or melancholic symptoms thyroidectomy offers less striking results. Implantations of radium have often given better results. Preference is given to local anesthetic preceded by morphia and hyoscine. One lobe, the isthmus and from a third to a half of the other lobe should be removed at operation. A working plan is to leave a fragment of thyroid about the size of one normal lobe. There was no tetany in this series. The remainder of the patients were improved in condition, and in the course of 3 to 4 months the pulse came down to 80 to 90. Often some cardiac dilatation remained. The tremor and irregularities of the pulse disappear and the exophthalmos recedes but does not disappear. The best results are obtained before cardiac changes have taken place. The basal metabolic rate drops from +40 to 80 or more to something over +25 in a few weeks.—R. E. K.

Isolation of the THYROID hormone (*Versuche zur Isolierung des Schilddrüsenhormones*). Romeis (B.), *Biochem. Ztschr* (Berl.), 1922, 132, 97-111.

Normal thyroid glands of freshly slaughtered sheep were minced, mixed with 10 times the amount of hot saturated $\text{Ba}(\text{OH})_2$ solution and cooked under a reflux condensor until no biuret reaction was given (12 to 14 days). The cooled extract was treated in 3 ways. The first method consisted in neutralizing with H_2SO_4 and filtering off the yellowish BaSO_4 precipitate. The filtrate and washings were concentrated on the water bath to a protein-free syrup. This material induced accelerated development of frog tadpoles, but slower than that caused by iodothylin. The second method consisted

of precipitating the Ba from the hydrolyzed extract by CO_2 and making the reaction alkaline with Na_2CO_3 . The BaCO_3 was removed by filtration and washed. The combined filtrates were concentrated and neutralized with acetic acid. The syrup was very active in promoting tadpole development, thus indicating that in neutralization with H_2SO_4 the greater part of the active principle is carried down with the BaSO_4 . The third method consisted of neutralizing the $\text{Ba}(\text{OH})_2$ with HCl . BaCl_2 remained in solution and the active part was precipitated out and filtered off after standing for several hours. Further purification was obtained by repeated solution in diluted NaOH and reprecipitation with acetic acid. Very small amounts of the dry precipitation sufficed markedly to accelerate tadpole development. Further purification was obtained by repeated extracting with 90% alcohol slightly acidified with acetic acid and evaporation of the alcohol from the filtrate. The final product was washed with water-free ether and petrol-ether. The product contained much iodine and appeared to be like thyroxin.—F. S. H.

Investigation on isolating **THYROID** gland hormones (Versuche zur Isolierung des Schilddrüsenhormones. 1. Teil). Romeis (B.), Arch. f. Entwcklungsmechn. d. Organ. (Berl.), 1922, 50, 410-467.

This is a report on 18 experiments in which a total of 805 tadpoles (mostly *Rana temporaria*) were used. It was found that an extract of the thyroid gland, purified, and having the albumin removed by several precipitations with absolute alcohol, causes in the tadpole experiment acceleration in development, but not the stimulation constantly noted on feeding with fresh thyroid gland. It is therefore a question whether this acceleration in development is to be considered as organically specific. The precipitate, rich in albumin, which comes down after the first alcohol precipitation causes a great stimulation, inhibits growth, and accelerates development. The purified substance from the alcohol extract, soluble in benzine, calls forth no acceleration in development. By extracting with 50% alcohol, acidulating with acetic acid and precipitating twice with acidulated 96% alcohol, it is possible to obtain from the fresh thyroid gland an alcoholic albumin-free extract fraction which causes stimulation, inhibits growth and accelerates development. The albuminous substances precipitated by acetic acid work the same way. The precipitates obtained by the first and second alcohol precipitation work only weakly (the first more than the second). The specific albumin-free extract portion, soluble in alcohol, is not soluble in benzine. It contains iodine. It may also be extracted from the fresh gland with 80-90% alcohol. The substance soluble in alcohol for the most part goes over into the acetone extract when acetone is used for dividing. But the division is not quantitative. By repeated operations the insoluble acetone portions causes inhibition of growth and acceleration of development. By shaking out the

acetone soluble extract with benzol, toluol, and trichlorethylen, the effective substance goes over into the extraction material only in traces or not at all. Even the substances separated from the extract with ether are not specifically effective when the shaking out occurs in aqueous solution in a neutral reaction and the extract obtained is once more taken up in pure ether after drying. The ether extract obtained in this manner contains cholesterin and a yellow unknown intermediate substance (probably corresponding to the "accompanying substance" of Wacker). Considerable numbers of effective substances go over into the ether extract when the extract in alcoholic solution is shaken out with ether. When this extract is dried and taken up in pure ether, the effective substance with a number of other substances remains insoluble. The substances (mostly cholesterin) dissolved in pure ether are not specifically effective. The residue containing iodine is for the most part soluble in neutral H_2O . The aqueous solution is very effective, also the scant precipitate which is soluble in weakly alkaline water. More abundant is the effective substance going over in the alcohol-ether-extract previously acidulated with H_2SO_4 . The specifically effective substances are precipitated by a sulphuric acid reaction from the purified albumin-free extract by phosphotungstic acid. It goes into the solution with barium when the phosphotungstic acid precipitate is decomposed. In the barium phosphotungstic acid precipitate there remains behind a substance to be extracted with $NaOH$ or NH_3 , which at neutralization precipitates for the most part and in the tadpole experiment retards growth without at the same time accelerating development. The substances going over into the filtrate and which are not precipitated by the phosphotungstic acid are not specifically effective. The effective substance precipitated by phosphotungstic acid and freed by barium hydroxide is soluble in 90% alcohol. The methods used do not show iodine in these substances. In spite of this it calls forth in the tadpole experiment the typical thyroid gland activity. After dissolving several times in 90% alcohol, small amounts of a crystallized substance could be obtained from weak sulphuric acid solution, a substance which in the tadpole experiment caused stimulation, checking of growth, and acceleration of development. As the absence of iodine indicates, this substance does not correspond with Kendall's thyroxine. The effective substance is further precipitated from the albumin-free extract by sublimate from neutral solution. Sublimate sodium acetate precipitates best. Alcoholic sublimate solution is also good. The substances that are not precipitated have no specific efficacy. The substance is not precipitated out by acid reaction. An aqueous thyroid gland extract made albumin free with aluminum silicate with acid reaction affects, in the tadpole experiment, growth and accelerates development. The efficacy of accelerated development is clearly distinguished from the typical thyroid gland activity by the absence of stimulation. The specific effective

substance is by this method separated at the same time as the albumin bodies. By shaking out one of the extracts made albumin-free with alcohol according to the above method with aluminum silicate, the effective substance is absorbed by aluminum silicate. The substances not absorbed have little or no specific efficacy. The absorbed effective substance may be extracted from the absorption medium by means of NaOH or NH_3 . The extract portion isolated in this manner is free from albumin, albumoses or peptones. It contains iodine. The substance obtained by neutralizing or acidulating this extract portion causes marked stimulation and moderate acceleration in development. Even the filtrate is still specifically effective. In the same manner as through aluminum silicate, the effective substance is adsorbed by animal charcoal. The filtrate has lost its specific efficacy. The substance adsorbed by aluminum silicate and dissolved in NaOH remains for the most part in the tube in dialysis through collodian membrane; but it is not albumoses. KIO_3 , KI , NaIO_3 , NaI and Lugol's solution in the tadpole experiment in dilutions of 1:50,000-1:500,000 cause neither acceleration of development nor retardation of growth. A stronger concentration is sometimes followed by death of the animal. Diiodotyrosine in only small doses (20-40 mg.) causes very distinct stimulation, acceleration in development, and checking of growth. The effect much resembles the symptoms appearing after strong thyroid gland feeding or administering of iodothyronine. In the very young *Esculentia* larvae the effect is much slower than with iodothyronine. Diiodotyramine, on the contrary, is weakly or not at all effective. The difference in the efficacy of diiodotyramine and diiodotyrosine depends on the presence of the carboxyl group; by substituting for them the amino group the specific efficacy is more or less lost. By these experiments it is shown that the specific efficacy of the thyroid gland feeding in tadpoles may be brought forth by an extracted albumin-free substance from the fresh gland. This is effective even if there is no longer a trace of iodine; but of course its efficacy is doubtless increased by the presence of iodine in a certain form of combination which is still unknown. The substance is abiuret, sulphur free and does not give a Millon reaction. The negative result of the Millon reaction would in the iodine-containing substance not contradict the presence of diiodotyrosine. But the test is also negative in the iodine-free preparation. The negative result of the Adamkiewicz-Hopkins test, which it was possible to confirm in some preparations without a distinction between their efficacy and that of a positive Adamkiewicz-Hopkins reaction, points to the absence of tryptophan complexes, which is of interest in view of the Kendall thyroxine which is a tryptophan derivative. Whether the isolated substance in the present experiment corresponds to the in vivo secreted hormone of the thyroid gland will have to be proved in further experiments, especially since it has not

THYROID and pregnancy (Corpo tiroide e gestazione). Vignes (E.), Med. prat. (Napoli), 1922, 7, 281-289.

A review. The author deduces that one of the functions of the thyroid is to insure oval nidation.—G. C.

THYROID action and fever. Ward (E. H. P.), Med. Rec. (N. Y.), 1921, 100, 399-407 (September).

The author states that the various actions of the thyroid secretion oppose those of adrenalin, and that the thyroid is responsible for rise of temperature in disease and the maintenance of normal temperature in health. The features of fever—throat vasodilation, full pulse, tachycardia, low blood pressure, headache, etc.—are all found to be in hyperthyroidism. Fever, therefore, is a manifestation of disturbance of balance between thyroid and adrenals.

—Prescriber, 16, 357.

(THYROID) Stridor caused by goiter (Ueber den Kropfstridor). Wiltshcke (F.), Wien. klin. Wchnschr., 1922, 35, 726.

Description of 4 infants in whom oppressed respiration was caused by a goiter. Best results were obtained by administration of small quantities of NaI.—J. K.

(THYROID) The dosage and technique in the x-ray treatment of goiter, tuberculous glands of the neck, tonsils and adenoids. Witherbee (W. D.), Am. J. Roentgenol. (N. Y.), 1922, 9, 514-516.

The author points out the association of infected tonsils, tuberculosis of the lungs and enlargement of the thyroid gland. He describes his treatment of these different conditions. His technique is as follows. Seven inch spark gap, 5 ma, 10 in. distance, 4 minutes time, filtered through 3 mm. of aluminum. The area of exposure for treatment of the thyroid extends from just above the external auditory meatus down to the lower level of the thyroid gland and transversely to the center of the middle lobe. Each side is given a four minute exposure, thereby including the tonsils and adenoids in a cross fire. The number of treatments is governed by basal metabolism determinations. The author has seen very favorable results, particularly in cases with infected tonsils. In no case was there evidence of impairment of the function of the thyroid or parathyroids.—J. C. D.

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PROGRESS IN THE PREPARATION OF PANCREATIC EXTRACTS FOR THE TREATMENT OF DIABETES*

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Seldom does science—medical science in particular—advance in perfectly straight lines, or by perfectly logical steps one directly above the other. In ascending the mountain of knowledge as in ascending physical mountains progress more often is accomplished by a zig-zag course. At times a mountain trail may seem to have lost the habit of ascending; it may even recede toward lower levels. And it is only by patiently threading one's way through obscuring growths at the base of the mountain, and then oftentimes after further baffling experiences in fogs about the higher levels, that one emerges finally to the clearer view and the immediate consciousness of achievement. Such has been the progress of understanding in the treatment of diabetes.

Not for a third of a century—not indeed since the demonstration by Minkowski and von Mehring (1) in 1889 that the seat of the disease is in the pancreas—had there been any really great advance in the rational treatment of this malady until about a year ago. The promise of Minkowski's work was instantly recognized and hopes were everywhere entertained that

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complete mastery was at hand. Encouraged by the results with dried thyroid substance or extract in the treatment of myxoedema, it was believed that administration of pancreatic substance must bring relief in the treatment of diabetes. But the Minkowski contribution only got us out of the woods; we were still a long way from the summit and apparently insurmountable barriers interposed. There were not wanting many who caught, or thought they caught, glimpses of a sure passage over the difficulties. But many of these glimpses proved wholly illusory; most of the passages had to be abandoned completely.

A year ago the medical and scientific world was thrilled by the announcement from Toronto (for reasons which will appear more clearly as I proceed one of us localized this thrill very near the solar plexus) to the effect that the internal secretion of the pancreas had at last been obtained in curative form and in quantity sufficient to control the major symptoms both of experimental and spontaneous diabetes. Minkowski and von Mehring's discovery had been based upon the complete extirpation of the pancreas from dogs, producing thereby a fatal condition alike in all essential respects to the disease in man. Banting and Best's (2) discovery was based upon ligation of the pancreatic ducts in the dog, thereby producing degeneration of the acinous tissue of the organ and rendering possible the extraction of the anti-diabetic substance produced by the islet cells in a state of purity and potency never previously attained.

As in mountain climbing, so in scientific pioneering the surest progress often is made by following up as far as it goes a trail blazed by somebody else. Failures may show up along the way, mistakes which appear utterly foolish in the light of newer experiences. This one has gone off on the wrong branch; that one has followed a false lead. But eventually comes along a bolder spirit or one of surer instinct, or, it may be by pure chance, the new wayfarer hits upon the right clue and amazingly and triumphantly he leads the way toward the summit. This is what Banting has done. If it be chance, however, which brings success, we must remember that "chance" in the words of Pasteur, "favors only the mind which is prepared." Nobody succeeds wholly by chance and nobody succeeds only because his mind is prepared. Pasteur himself illustrates the importance of another element, namely, persistence; and this quality is well

exemplified also by Banting, who labored against discouragements for many months before he succeeded in convincing others that he was on the right track.

It is a mistake to suppose that some progress had not been made before this time—that pancreatic extracts had never been prepared or that they had not been used with some success on human cases. It is no discredit to Banting and his colleagues; rather the contrary, to recall that more than a dozen scientific investigations had been carried out with pancreatic material which diminished the excretion of sugar in either depancreatized dogs or human cases of severe diabetes or both before these investigators reported success. In several instances these preparations caused the complete disappearance of sugar from the urine, caused increase in weight, and general improvement in the clinical condition of the patient. But most of these attempts had to be abandoned because of toxic or other deleterious results which overshadowed the benefits gained.

Because we often learn more from a failure than from a success let me review *briefly* the history of these researches. Minkowski (3) himself, the next year after the publication of his completed experiments on extirpation in 1892, tried to make an extract of dog's pancreas which, when injected into the animal from which it had been taken would restore his power to metabolize sugar. He failed completely. Even before Minkowski, but stimulated by his discovery, Caparelli (4) made an extract of dog's pancreas in 0.76% NaCl solution which, when injected into the peritoneal cavity of a dog caused an abrupt fall in the excretion of sugar within three hours and in most instances complete disappearance soon thereafter. In 1893 also, clinical trials of pancreatic material were made by Ballistini (5) in Italy, and by Ralfe (6), Sibley (7), Wood (8), Mackenzie (9) and White (10) in England. Ballistini, Sibley and Ralfe reported some success; the others reported failures. Some of them gave fresh pancreas or pancreas slightly cooked, by mouth, some gave press juice and some extracts. In 1895 there were positive reports by Ausset (11) in France, and Bormann (12) in Russia, negative results by Vanni and Burzagli (13) in Italy. Ausset used raw pancreas of veal upon a depancreatized dog and a single human subject. Bormann used roast pancreas by mouth, later rectal infusions, and finally subcutaneous injections of raw

pancreas. One of his patients who received 1.5 cc. of pancreatic extract daily under the skin gained eight pounds in six weeks, the diet remaining substantially the same. Vanni and Burzagli used a glycerine extract and also raw pancreatic extract given subcutaneously. There was no clearly favorable result.

In 1896 there was one report upon each side of the controversy. Lissner (14) reported from Odessa that rectal infusions made from hashed fresh pancreas with normal saline solution caused marked diminution both of the glycosuria and polyuria. One subject gained 2.5 kgm. in weight, the other 4 kgm.; but in the latter case the infusions could not be tolerated longer. Spillmann (15) reported two subjects treated by injection with pancreatic press juice. There was only slight abatement of the glycosuria.

In 1897 Thesen (16) and Lauritzen (17) found favorable effects in human cases, the former feeding 50 to 300 gms. of raw pancreas daily, the latter a glycerine extract given by mouth. Thesen found, as many others have found since, that raw pancreas soon becomes repugnant. This year also a notable piece of work was done by Hougounenq and Doyon (18) upon depancreatized dogs. They made extracts in a great variety of ways, but were not able to demonstrate any beneficial effects when they were administered to the diabetic dogs by stomach. This well-controlled work made a marked impression on clinicians and very considerably discouraged the use of pancreatic material in any form by mouth; particularly as it was followed the next year by the observations of Hédou (19) to the effect that glycerine extract given by mouth to depancreatized dogs likewise produced almost no effect. Blumenthal (20), however, saved the record for 1898 by squeezing out the juice from raw pancreas in much the same way, though not employing such high pressures, as Buchner had used in obtaining zymase from yeast. He precipitated the proteins from this juice with alcohol and gave the filtrate to animals as well as to human subjects. Given intravenously it killed his animals but caused only necrosis at the site of injections when given subcutaneously either to animals or men with fatal diabetes. In one case he reports 40 per cent increase in the combustion (meaning utilization) of sugar. It is obvious why he discontinued its use. Nevertheless Blumenthal was on the right track.

Another significant observation this year (1898) was that of Lépine and Martz (21), who examined the lymph of a normal dog and found a substance capable, when injected intravenously into a rabbit, of causing marked glycolysis, i. e., disappearance of sugar from its blood. Although Lépine's idea of a ferment (glycolysin) later proved unacceptable, Biedl and Offer (22) several years later confirmed the significance of his observation on the thoracic lymph by showing that exclusion of the duct lymph from the circulation by ligation or by fistula produced profound glycosuria.

With one exception (23) all attempts (24, 25) made in the next ten years resulted negatively. In 1903 Rennie (26) reported upon the interesting occurrence of an entirely separate pancreatic organ for internal secretion in teleostean fishes, and four years later Rennie and Frazer (27) undertook the treatment of diabetes mellitus by feeding this islet material, but without avail. Lépine is the only outstanding worker who seemed never to lose faith in the ultimate solution along the lines of his glycolytic ferment. He believed the pancreas produced a substance (ferment) which it gave off mainly to the lymph rather than the blood, and that this ferment was the *sine qua non* for the breakdown of sugar, the absence or failure of which produced diabetes. Here should be mentioned the observations of Cohnheim (28) confirmed by Hall (29) upon the disappearance of sugar *in vitro* when pancreatic extract together with muscle plasma was allowed to act upon it at incubation temperature. Cohnheim at first thought this was a true oxidation, but Levene and Meyer (30) proved that the loss of reducing power was due to a process of polymerization; for all of the sugar could be recovered when the mixture was hydrolyzed with hydrochloric acid.

Meantime by a process of attrition rather than by direct assault another important vantage point was gained. Observations were accumulating which rendered more and more probable the causal relation of the islet tissue to diabetes, first enunciated by Laguesse (31). Atrophy of the acinous tissue without change in the islets produced by ligation of the ducts, was first noted by Vassale (32) and was confirmed among others by Schultz (33), Ssobolew (34), Sauerbeck (35), Tiberti (36), Kirkbride (37) and Kamimura (38). Pathological changes in the

islet cells in cases of human diabetes have been described by Opie (39), Ssobolew (34), Herzog (40), Weichselbaum and Stangl (41), Gutman (42), Cecil (43) and others. While there is no unanimity of opinion as yet regarding the evidence from pathological material, the recent experiments of Allen (44) upon partially depancreatized dogs with production of hyaline degeneration in the B cells of the islets, coincident with a breakdown of carbohydrate tolerance, appear to place the dependence upon surer grounds.

This period from 1898 to 1908 was marked also by the development of the dietary treatment of diabetes and by the inauguration of almost endless researches upon the metabolism of diabetes which have by no means exhausted the subject even yet. The salient points for our present purpose established by these investigations are the following: (1) The primary defect in diabetes is not the excessive production of sugar but the inability of the organism to oxidize it. (2) This condition is signalized ordinarily by the attainment of a certain ratio (3.65 of glucose to 1 of nitrogen in the urine, the glucose being in excess of the glucose equivalent ingested); also by the attainment of a respiratory quotient of 0.69. (3) To attain these numerical levels the diabetic excretes all the sugar which is formed in the course of the metabolism of protein (as well as all his carbohydrate) and this amounts to as much as 60 per cent of its weight. (4) There is an excessive heat production in diabetes which is caused by the increased metabolism of protein. (5) The acidosis of diabetes arises from the inability of the diabetic to complete the oxidation of fatty acids and certain amino acids, with the result that these acids are excreted (aciduria) but especially also they deplete the reserves of alkali in the body (true acidosis). (6) Much information has been gained in recent years also upon the blood sugar in diabetes, its relation to sugar excretion, to dietary and starvation treatment, etc. So that we have today three main chemical criteria as to the condition of a diabetic: (1) the D:N ratio in the urine, first insisted upon and developed by Lusk; (2) the blood sugar level, standardized for the normal individual mainly by Benedict at Cornell, Folin at Harvard and Shaffer at St. Louis, and turned to account in the study of diabetes chiefly by Joslin at Boston, by Woodyatt at Chicago, and by Allen at Morristown,

and (3) the respiratory quotient first established for the diabetic by Magnus-Levy and confirmed by Kramer and myself for the dog and by DuBois and by Boothby for man. It may be mentioned in passing that the respiratory quotient is much more difficult to establish than the other criteria, and it is correspondingly more difficult to demonstrate a change in the respiratory quotient when any treatment for diabetes is being given. At the same time it is the best criterion of all of real improvement: *for unless you have restored your patient's capacity to oxidize glucose you have done him no permanent good.*

But to resume the story of the development of pancreatic therapy: Pfüger, in his famous controversy with Minkowski regarding the nature of diabetes, laid down the principle that an internal secretion is not proved by extirpation alone. One must be able also to restore lost function by administration of the organ substance, as was known even at this time for the thyroid, or an extract of the organ as in the case of the adrenals. Zuelzer (45, 46), in 1908, guided by this principle, and impelled by the belief that previous attempts with pancreatic material may have failed because of the condition of the pancreas at the time of extraction, made a very determined effort to prepare from perfectly fresh material an extract which should exhibit anti-diabetic properties and thereby to establish the fact that the pancreas accomplishes its work by means of a hormone. The term "hormone," by the way, had been introduced only a couple of years before by Bayliss and Starling in connection with their work on sécretin. Zuelzer's efforts were all but successful. He took pancreas at the height of digestion, tied it off for an hour and a half, then removed and extracted it, squeezed out the juice, precipitated the proteins by means of alcohol, until there was scarcely any biuret reaction left, and administered the alcohol-free extract subcutaneously and intravenously. With depancreatized dogs he saw the sugar excretion fall off sharply or disappear. He reports eight human cases treated. Several of the subjects were obviously improved as regards excretion of sugar. One became sugar free, in spite of 100 grams bread in the diet, and remained so for four days from a single injection of 10 cc. of the extract. One of his cases was that of a boy six years of age who received a single injection of 5 cc. by vein. The urinary sugar dropped from 4.4% to 2.6% and both diacetic

acid and acetone disappeared from the urine. The child, however, showed a marked temperature reaction and was severely nauseated. For these reasons, apparently, the treatment was discontinued. Zuelzer's results, however, were confirmed the next year, 1909, by Forschbach (47), who published results on several depancreatized dogs and in some half-dozen human cases. Like Zuelzer, he was discouraged by febrile reactions.

Many times in the search for a satisfactory pancreatic therapy it has been reported (48, 49) that, so far from controlling diabetes, fresh pancreatic material aggravated the glycosuria. Leschke (50) in 1910 investigated the cause of this phenomenon which he had observed in frogs, by administering aqueous pancreatic extract which had been heated to 70° C. *for the purpose of destroying the external enzymes*. The heated material did not have the effect which he had seen with raw extracts. The latter in mammoth doses even caused glycosuria in normal animals. He concluded that the enzymes were responsible for the unfavorable effects. Allen (51) has shown that the glucosuric effect of pancreas extract injected in this way is not specific but is shared by other organs such as liver and skeletal muscle. Curiously enough Leschke thought his observations refuted the whole conception of an internal secretion, and he was so biased in this preconception as to be quite unfair in his review of results obtained by previous investigators. Allen seemed ten years ago to have borrowed Leschke's views.

Without doubt one cause for the many failures to produce a satisfactory extract up to this time had been the destruction of the hormone by the external enzymes (trypsin) of the pancreas itself or by pepsin when the pancreatic material was given by stomach. This idea was first acted upon by Croftan (52), who in 1910 prepared an extract from the press juice of pig's pancreas and heated it for three hours at 80° C. Trypsin was completely inactivated. The extract was filtered, mixed with 25 per cent glycerine for preservation and was fed with some success to diabetic patients. The next year, 1911, E. L. Scott (53) undertook to eliminate the external enzymes by ligation of the ducts and degeneration of the acinous tissue in exactly the manner employed by Banting and Best. He did not succeed in occluding the ducts completely, consequently never prepared

an extract of degenerated pancreas. He sought to accomplish the same end, however, by extraction with alcohol, and when this extract proved unserviceable on account of depressor substances, he employed an acidulated aqueous medium which lowered the D:N ratio in depancreatized dogs quite significantly.

The same year Pratt and Spooner (54) fed fresh pancreas to a dog with very much reduced carbohydrate tolerance, brought about by complete isolation of the pancreas from the intestine. They succeeded in raising his tolerance by continued pancreas feeding considerably beyond the average normal level. The next advance in our knowledge of the internal function of the pancreas grew out of Bayliss and Starling's work on secretin. Knowlton and Starling (55), working in Starling's laboratory in London, found that an extract of pancreas made in acid solution after the manner of preparing secretin enabled the heart of a diabetic dog to metabolize sugar. This result was speedily confirmed by McLean and Smedley (56) at the Lister Institute. But upon attempting to repeat the observations in conjunction with Patterson (57), Starling failed and concluded that his previous experiments with Knowlton had been defective.

It was at this point that the writer's interest became aroused at Cornell Medical College. Before Knowlton and Starling published their results the idea that the duodenal lining might have something to do with the production of the internal secretion as well as with the external secretion of the pancreas suggested itself. Accordingly a combined extract of pancreas and duodenal mucosa was prepared. It stood about the laboratory for months. Finally an opportunity came to try it on a diabetic and, happily, the extract diminished his excretion of sugar. Having in mind some of the great difficulties which had been encountered by previous workers, and especially Pflüger's principle that the internal secretion should first be proved by application to the depancreatized animal, Kramer and I (58) in 1912 set to work upon the problem, employing first the method of extraction of Knowlton and Starling, which by this time had been published. One of the first experiments performed, but with an extract prepared in much stronger acid, succeeded so well that after neutralization and boiling, upon injection into the vein of a diabetic dog it caused the urine to become sugar free in a little more than two hours and to remain

so for six hours. But alas! when next day the total excretion for the entire twenty-four hours was balanced up it was found that the dog gave back all the sugar which had disappeared from the urine and it looked as if the extract only blocked the kidney outlet temporarily. It is now almost certain from Macleod's (59) results that the true explanation lay in the temporary storage of glycogen. The idea that the duodenum contributes something to the formation of the pancreatic hormone has not proved fruitful.

The experiments were continued, and with further successes, but new difficulties were encountered. Everybody at this time thought it was unphysiological to give an extract or any foreign fluid by vein unless it were made alkaline and the apparent effect on the kidney, it was feared, might have been due to unneutralized acid; hence not only was the acid employed in extraction neutralized as had been done in the first experiments, but the fluid was made distinctly alkaline with sodium carbonate. This was the fatal step, for the anti-diabetic substance was destroyed or at least obscured by using too much alkali.

This, however, was not the end of our work. Finding that alkali alone (1% sodium carbonate) would reduce the excretion of sugar, the problem was pursued as opportunity afforded for three years, and finally in 1916, after it had been demonstrated conclusively that alkali did not cause the storage of glycogen (60) or combustion of sugar, although it might improve the conditions for oxidation in the partially depancreatized animal, pancreatic extract was once more employed. This time it was shown that an acid extract made slightly alkaline and given with sugar into the stomach of a depancreatized dog did actually cause the oxidation of sugar (61).

Kleiner and Meltzer (62) meantime had shown that finely-ground suspensions of pancreatic gland in sterile water would bring about a reduction of the blood sugar in depancreatized dogs. Their preliminary results were reported while Murlin and Kramer were engaged upon the problem and one of the depancreatized animals used by the latter was given a suspension of pancreas intravenously and subcutaneously with the result that the respiratory quotient was raised some ten points. This particular experiment has only recently been published (63). Several years later in reporting their completed experiments,

Kleiner (64) erroneously quoted Murlin and Kramer as having "always used an alkaline medium." It should be made clear that Murlin and Kramer's extracts were, in the great majority of cases prepared in acid media, but were neutralized or made alkaline before administration. Furthermore, it was shown that in totally depancreatized animals the alkali alone never raised the respiratory quotient more than two or three points, whereas the combined extract (made in acid) and weak alkali (N/20 NaOH final reaction) increased the quotient several times to ten points and once eighteen points (0.87). This result obtained in exactly the same manner has recently been confirmed many times. There was also in the earlier experiments an increased heat production and prolongation of life from this treatment.

Macleod (65) and his colleagues have been in error in supposing that these results were not considered sufficiently constant or significant "to justify more intensive research with the object of securing preparations of greater potency that could be used for treatment of diabetes in man." It was with exactly this object that work was resumed at the University of Rochester a year ago last October, as soon as a new laboratory could be organized for study of all the important criteria. Work was well under way before it was known that Dr. Banting and Dr. Macleod were interested in the problem. Nothing was known of their results beyond the fact that Banting had employed ligation of the ducts and extraction of the degenerated pancreas, until Banting and Best's first paper (delayed in reaching the laboratory) came to the writer's attention in April, 1922. By this time further favorable results upon the respiratory quotient with extracts and entirely new results with perfusates of pancreas had been obtained. These facts are stated merely for the purpose of making it clear that the results up to this point obtained at Rochester were in no way dependent upon the successes at Toronto. They therefore constitute a much more significant confirmation than would otherwise be the case.

Before recapitulating what has been accomplished the past year and a half mention should be made at this point of the favorable results reported by Paulesco (66). They were distinctly encouraging. He found that the intravenous injection of a sterile extract into depancreatized dogs brought about a diminution or even a temporary suspension of the hypergly-

cæmia and of the glycosuria; also a diminution of the excessive production and excretion of urea and acetone bodies. The effect, he found, appeared immediately, reached its maximum in about two hours, and continued for twelve hours. The method of preparation employed by Paulesco has not been available to the writer.

Banting and Best's results may be summarized briefly as follows. Extract of pancreas caused to degenerate by ligation of the ducts brings about a sharp drop in the hyperglycæmia and glycosuria of depancreatized dogs. Extract of fetal pancreas does the same. These successes led to a re-examination of the methods of extraction of adult pancreas and it was found that a slight modification of Scott's method gave an extract which upon concentration produced a very powerful anti-diabetic effect, particularly after dialysis. Collip (67) improved upon the method of extraction and purification and the resulting extract in concentrated form was first used with human cases of diabetes in January, 1922. Up to February 22nd it had been tried with hopeful results in seven cases (68).

Following the joint report of Banting, Macleod and their colleagues to the Association of American Physicians (69) and to the Royal Society of Canada (68), interest in their results has become widespread. Schafer (70) in 1916 suggested the name *insuline* for the active principle of the internal secretion of the pancreas. This name (without the final "e") has been adopted by the Toronto physiologists, but they appear to have limited its use to the alcoholic extract. In addition to the demonstration of reduced hyperglycæmia and diminished glycosuria in depancreatized dogs and human cases, Macleod, Banting and their colleagues have now shown that the respiratory quotient may be raised by injections of *insulin* to a level indicating beyond a doubt the combustion of carbohydrate (68). They have also shown that *insulin* will reduce the blood sugar in normal rabbits, will counteract the effect of epinephrin, asphyxia, etc., and will increase the glycogen content of the liver and diminish the excretion of ketone bodies in depancreatized dogs (59). More recently (71) the Toronto workers have undertaken to standardize their *insulin* (which they define as a purified alcoholic extract of pancreas) by the blood sugar test on normal rabbits, while Hepburn and Latchford (72) from the same laboratory

have added the interesting information that under its influence the normal rabbit heart may be induced to increase its consumption of sugar from a normal rate of 0.87 mgm. per gram per hour to 3.06 mgm.—nearly four-fold. More detailed data regarding the antagonistic effect of *insulin* against the hyperglycæmia of piqure, epinephrin, mechanical and carbon monoxide asphyxia and ether constitute the latest of these most important contributions.

When the first authentic reports from Toronto reached the Rochester laboratory it was seen that they contained confirmation of the method of extraction employed by Murlin and Kramer in 1913-1916. The essence of this method lay in the use of acid in sufficient amount to restrain the action of trypsin. Murlin and Kramer (63) had been led to increase the strength of the acid above that used by Knowlton and Starling because of the fact that signs of the effects of active trypsin had been seen when the extracts were given subcutaneously. Our work started off in 1921 with the use of similar extracts and we had two good experiments (73) showing marked increase in the respiratory quotient before we knew anything of the Toronto results. But we were having the same difficulties from toxic effects that the Toronto workers were having, and to obviate these we were trying the perfusion method introduced by Clark (74) when the results of Banting and Best first came to our hands. Their experience stimulated us to try more prolonged extraction and to adopt an acid (76) instead of an alkaline (75) reaction in the perfusion fluid. We soon found that we could obtain highly potent preparations by either method and that they could be administered after careful neutralization to depancreatized dogs subcutaneously, intravenously or intraperitoneally without toxic effects. Dogs rendered totally diabetic by extirpation of the pancreas under treatment, even with unconcentrated extracts, immediately exhibited improvement in all the cardinal symptoms. The blood sugar could be brought down precipitately to normal or below, the urine could be rendered sugar-free, and the respiratory quotient could be raised to 0.90 or higher by means of one or two doses. Comparison (73) was made between this aqueous method of extraction and that published by Collip in May, 1922, and it was found that with equivalent concentration the simple aqueous extraction gave results just as favorable

as the alcoholic extraction *with the advantage that toxic effects* (on dogs) *were not so frequent*. On July 17, 1922, the extract was first administered to human subjects by duodenal tube. One case (77) in particular which is shown in the chart, exhibited marked improvement as regards blood and urinary findings from this method of administration. But upon resorting to subcutaneous administration of more concentrated and more highly purified extracts the improvement was still more rapid. A number of other patients have been given the extract subcutaneously and at the time of writing there have been for several months no unfavorable effects, while the cardinal symptoms have been almost wholly eliminated. The smallest effective dose thus far (i. e., the most potent extract) was 0.5 cc. More recently even more concentrated extracts have been prepared.

Potent extracts of dog's and cat's pancreas had been prepared by perfusion (75) of a faintly alkaline Locke's solution through the pancreatico-duodenal artery. But the potency was increased when the 0.2% sodium bicarbonate was replaced with 0.2% HCl. Even without concentration these perfusates contain a sufficient quantity of the anti-diabetic substance to reduce the blood sugar, stop the excretion of sugar through the urine, and raise the respiratory quotient when given subcutaneously to depancreatized dogs in doses of 25 cc. In purified form they have also proved very potent with human cases.

The perfusion method has two advantages over any extraction method yet tried by us: (1) it yields a fluid containing considerably more of the anti-diabetic substance per unit weight of pancreas; and (2) this fluid contains relatively little extraneous protein. A method of percolation recently worked out at Rochester accomplishes the same result as perfusion but at a more rapid rate. All extracts contain a substance which will raise the blood sugar of normal rabbits or depancreatized dogs and unless this substance is removed one does not obtain the full potency of the extract. Only once out of 40 perfusions of cat, dog, pig and ox pancreas have we encountered this property in the perfusate.

Recent experiments show that the anti-diabetic substance can be precipitated (78) by means of trichloroacetic acid, or acetone, or by pure ethyl, propyl, butyl and amyl alcohols, or can be salted out by means of ammonium sulphate or sodium

chloride. It is resistant to heat up to boiling temperature (79); it does not dialyze rapidly and therefore can be freed of salts, and it remains potent in slightly acid medium for at least four months. Both the solubility and stability are exceedingly sensitive to the H-ion concentration. We do not believe the potent substance is a protein; for we get potency in the complete absence of the biuret and other protein reactions and in some in-

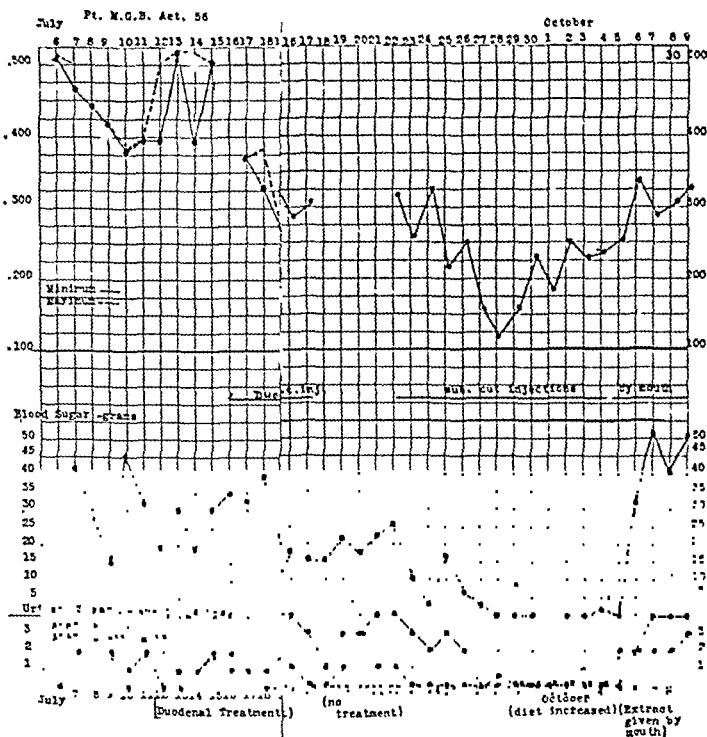


Chart showing of diabetes mellitus treated successfully first by du mouth. The double curve in the upper part of the

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CLASSIFICATION AND TREATMENT OF HYPOPHYSEAL DISORDERS*

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Experimental evidence, including injection experimentation, extirpation, etc., has given remarkably contradictory effects. Some workers ascribe certain functions to one lobe, and others the same function to a different lobe; and still others ascribe all resultant disturbance to perihypophyseal injury, or to the stalk alone. Out of this heterogeneous mass of contradictory evidence have come many classifications. The most notable classification is that of Cushing (1), which describes all conditions of perverted pituitary function as dyspituitarism, subdivided into five groups:

Group I. Cases of dyspituitarism in which not only the signs indicating distortion of neighboring structures, but also the symptoms betraying the effects of altered glandular activity, are prominent;

Group II. Cases in which the neighborhood manifestations are pronounced, but the glandular symptoms are absent or inconspicuous;

Group III. Cases in which neighborhood manifestations are absent or inconspicuous, though glandular symptoms are pronounced and unmistakable;

Group IV. Cases in which obvious distant cerebral lesions are accompanied by symptomatic indications of secondary pituitary involvement;

Group V. Cases with a polyglandular syndrome in which the functional disturbances on the part of the hypophysis are merely one, and not a predominant feature of a general involvement of the ductless glands.

"Under each of the first four groups, there will naturally occur three subdivisions: namely (1) the cases in which the clinical manifestations of past or of existing hyperpituitarism predominate (more particularly overgrowth, resulting in gigantism when the process antedates ossification of the epiphyses—typus Launois; resulting in acromegaly when it is of later occurrence—typus Marie); (2) those in which the clinical manifestations of hypopituitarism predominate (adiposity, with a persistence of both skeletal and sexual infantilism when the process originates in childhood—typus Froehlich); adiposity with sexual infantilism of the reversible form when it originates in the adult—the type we have explained on experimental grounds and of which clinical illustrations are to be given); and (3) the mixed or transition cases exhibiting some features of both states—in other words, with evident dyspituitarism."

Bell (2) states: "From a scientific point of view, as well as for the sake of lucidity, it appears to me better to consider

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pituitary lesions as primary, and as secondary to disease in the neighborhood, to general disorders or to derangements of the other organs of internal secretion; and, also, in each case according to whether there is a condition of excess of secretion or deficiency—so far, at any rate, as our knowledge will allow such an estimation.”

Timme (3) suggests as the best classification for purposes of therapy, one based upon a primary division depending upon the characteristics of the sella turcica, with secondary qualifications in each division, based upon the symptomatology. Our main objection to this classification would be the fact that such a large percentage of cases showing gross evidence of pituitary disturbance, show no changes in the sella turcica.

In an attempt at still greater lucidity, and feeling that the consensus of experimental, pathological, and clinical evidence justifies the conclusions at least tentatively, Engelbach and the author have devised a classification embodying the supposed functions of the individual lobes (4), (5). The clinical material, including a study from every possible angle, the response to therapy, etc., consisted at the time of the original classification of 892 endocrine cases, of which 147 were diagnosed as disorders of the pituitary gland; 350, of the thyroid; 194, of the gonads; 186, pluriglandular disorders; 10, diseases of the adrenals; and 5, thymus diseases. Of the 123 hypopituitary cases, 23 were grouped as anterior lobe; 3, as posterior lobe; and 86, as bilobar insufficiencies. The hyperpituitarisms totaled 24, of which 6 were anterior lobe; 2, posterior lobe; and 16, bilobar varieties. There were 11 cases of diabetes insipidus, some of which were associated with clinical signs of anterior lobe and posterior lobe symptoms. Pituitarism as a part of a pluriglandular complex (not included in the 147 primary pituitary disorders) occurred in 122, making a total of 269 cases in which clinical manifestations of pituitarism were present. At the present time, this material has been markedly increased, the total number of cases studied to date being 1995.

At the present time, although realizing the tentative character of the classification, the essentially questionable hypothesis, and the fact that changes necessarily will be made, we feel that we do not care to modify it. In this classification the hypophysis is considered as consisting of two lobes, the anterior and the pos-

TABLE I

HARMONIC SIGNS OF THE ANTERIOR LOBE OF THE HYPOPHYSIS

		HYPOPHYSITARISM		HYPERPHYSITARISM	
A. Osseous		HYPOPHYSITARISM		HYPERPHYSITARISM	
		Preadolescent A. Undergrowth. All Bones LORAIN-LEVI type	Postadolescent and flat bones. Short. only. (Normal long bones)	Preadolescent A. Overgrowth. Acranial, short and flat bones only. (Long bones short) Acromegaly	Postadolescent A. Overgrowth. Acranial, short and flat bones only. (Long bones short) Acromegaly
1. Stature					
a. Measurements		1. Short a. Torso greater than lower. Span less than height	1. Tall, or normal a. Varies. Torso greater than lower or less than lower (eu- nuchoid)	Gigantism Normal giant Eunuchoid giant Acromegalic giant 1. Abnormally tall a. Normal giant: torso=lower, span=height Eunuchoid giant: torso less than lower, span greater than height Acromegalic giant: torso greater than lower, span less than height	1. Short and stocky, or normal a. Acromegaly: torso greater than lower, span less than height
2. Head		2. Small a. Small b. Pointed, straight	2. Small a. Small b. Pointed, straight		2. Large a. Large b. Blunt, rounded
c. Superior Maxilla		c. Normal	c. Normal		c. Prominent
d. Chin		d. Pointed, sharp	d. Pointed, sharp		d. Rounded, blunt. Prog-
e. Sella Turcica (X-ray)		e. Small, except neoplastic type enlarged	e. Small, except neoplastic type enlarged		e. Normal, except neoplastic type enlarged
3. Hands		3. Type "en petit," one-third smaller than normal	3. Small	3. Type "en longe," one-third larger than normal. No dis- proportion	3. Type "en large," spade hand, wrist wide, fingers broad and clubbed. Infiltration of soft tissues over bones. Hands and head involved
a. Phalanges (X-ray)		a. Narrow, taper- ing, tuberosities and tufting ab- sent	a. Narrow, taper- ing tuberosities and tufting ab- sent	a. Wide, dense, tuberosities large, terminal tufting, ex- ostoses	a. Wide, dense, tuberosities large, terminal tufting, ex- ostoses
4. Pelvis		4. Broad, feminine type	4. Broad, feminine type	4. Narrow, masculine type	4. Narrow, masculine type
a. Genu		a. Valgum	a. Valgum	a. Varum	a. Varum

B. Genital	1. Gonads (ovary or testicle)	2. Uterus	3. Menses	B.		B.		B.	
				1. Infantile	2. Normal	1. Normal	2. Normal	1. Large, well developed	2. Normal
4. Sterility and Impotence	Present	4. Present	4. Present	2. Normal	3. Normal	2. Normal	3. Normal	3. Normal	3. Normal
5. Secondary Sex Characters	5. Absent	5. Absent	5. Present	3. Amenorrhea, metrorrhagia, and dysmenorrhea	3. Normal	3. Normal	3. Normal	4. Absent (present after many years with transition to hypopactivity)	4. Absent (present after many years with transition to hypopactivity)
C. Muscular	C. Proportionate to development	C. Proportionate to development	C. Normal	4. Present	4. Absent (present in a few years with transition to hypopactivity)	4. Absent (present in a few years with transition to hypopactivity)	4. Absent (present in a few years with transition to hypopactivity)	5. Present (even after hypopactivity occurs)	5. Present (even after hypopactivity occurs)
1. Muscle Tonus	1. Normal	1. Normal	1. Fatigability frequent	5. Absent	5. Present (even after hypopactivity occurs)	5. Present (even after hypopactivity occurs)	5. Present (even after hypopactivity occurs)	C. Overdeveloped	C. Overdeveloped
D. Mental	D. Usually deficient or retarded	D. Usually deficient or retarded	D. Average	6. Proportionate to development	6. Proportionate to development	6. Proportionate to development	6. Proportionate to development	1. Retained after age of 40-45	1. Retained after age of 40-45
E. Dermal	a. Upper incisors enlarged, lateral occlusion good	a. Upper incisors enlarged, lateral occlusion good	a. Occasional separation and frequent enlargement of upper incisors	7. Proportionate to development	7. Proportionate to development	7. Proportionate to development	7. Proportionate to development	D. Abnormally developed, temperamental, loquacious, unstable	D. Abnormally developed, temperamental, loquacious, unstable
b. Hair Distribution	b. Absent	b. Absent	b. Normal	8. Proportionate to development	8. Proportionate to development	8. Proportionate to development	8. Proportionate to development	a. Separation of upper incisors constantly; frequently lower, with prognathism	a. Separation of upper incisors constantly; frequently lower, with prognathism
F. Temperature	F. Subnormal	F. Subnormal	F. Normal	9. Proportionate to development	9. Proportionate to development	9. Proportionate to development	9. Proportionate to development	b. Marked increase on extremities and chest	b. Marked increase on extremities and chest
G. Pulse	G. Slow	G. Slow	G. Slow	10. Proportionate to development	10. Proportionate to development	10. Proportionate to development	10. Proportionate to development	F. Normal	F. Normal
H. Blood-pressure	H. Hypotension, or normal	H. Hypotension, or normal	H. Hypotension, or normal	11. Proportionate to development	11. Proportionate to development	11. Proportionate to development	11. Proportionate to development	G. Normal, or above normal	G. Normal, or above normal
				12. Proportionate to development	12. Proportionate to development	12. Proportionate to development	12. Proportionate to development	H. Normal, or above normal	H. Normal, or above normal

terior, with the pars intermedia as a part of the latter. The functions of the individual lobes, acting through their secretory hormones, have been considered as follows: (1) the anterior lobe regulates and controls (a) the skeletal growth and (b) the function and development of the gonads and the secondary sex characters; (2) the posterior lobe is concerned with (a) the regulation of the carbohydrate metabolism (glycosuria, hyperglycemia, sugar tolerance, and obesity), (b) the contraction of the involuntary unstriated muscles (persistalis and uterine contraction), (c) the renal secretions (polyuria), (d) the blood pressure, and (e) the body temperature. There are unquestionably many other minor functions of these lobes which are too indefinite to serve as valuable clinical evidence of activity. Reciprocal relationships undoubtedly will enter, but if present to a decided degree, usually can be recognized by their individual clinical manifestations. The syndromes, exclusive of pituitary neighborhood signs and symptoms, formerly termed glandular symptoms, are designated *hormonic* signs and symptoms, a qualification applying to all endocrine disorders. These *hormonic* signs and symptoms are defined as physical or metabolic changes, associated with other endocrine symptoms, due to an abnormal secretion of a ductless gland. Those pertaining to pituitary disorder are divided into physical, metabolic, and other endocrine symptoms. The physical *hormonic* signs are subdivided into regional and general. The general and regional signs can best be appreciated from the appended tables.

The neighborhood signs and symptoms, while important as diagnostic evidence of the neoplastic varieties and disorders, were of little value in differentiating varieties and types for the purpose of classification for diagnosis; and pituitary tumors were found associated with all types of clinical disorder, and, on the other hand, all clinical types were seen without evidence of tumor. Cushing (1) and Timme (3) both call attention to the not infrequent occurrence of a normal sella in pituitary disease. Furthermore, the incidence of pituitary tumor was so rare (about 6 per cent), that this symptomatology was practically useless as a basis for general classification; and up to the present, the histopathology of the pituitary in the absence of tumor is so meager and poorly defined that it is not dependable as a basis for classification, although we feel that the future will offer

TABLE II

HORMONIC SIGNS OF THE POSTERIOR LOBE OF THE HYPOPHYSIS

	HYPOPITUITARISM	HYPERPITUITARISM
I. Metabolism	I.	I.
a. Basal Metabolism	a. Decreased	a. Increased
b. Carbohydrate Tolerance	b. Increased	b. Decreased
c. Glycosuria and Hyperglycemia	c. Absent	c. Present
II. Adiposity	II. Marked girdle,mons and mammary	II. Absent, usually emaciation
III. Polyuria	III. Present (Pars Intermedia?)	III. Absent (or present with glycosuria)
IV. Involuntary Muscle Contraction	IV.	IV.
a. Intestinal	a. Absent; frequent intestinal atony	a. Present; frequent intestinal spasticity
b. Uterine	b. Absent	b. Present
V. Endocrine Secretion	V.	V.
a. Thyroid	a. Hypoactivity (hibernation)	a. Hyperactivity
b. Adrenals	b. Insufficiency?	b. Hyperactivity
c. Gonads	c. Hypoactivity (with Anterior Lobe disorder)	c. Hyperactivity (with Anterior Lobe disorder)
d. Pancreas	d. Normal (increased sugar tolerance)	d. Hypoactivity (decreased sugar tolerance)
VI. Nervous	VI. Apathy; Somnolence frequent	VI. Psychic instability
VII. Temperature	VII. Subnormal	VII. Normal
VIII. Pulse	VIII. Slow	VIII. Rapid

something more definite along this line. The unimportance of actual tumefaction in pituitary disease may be appreciated when we consider the fact that we recognize clinically hyperthyroidism in the absence of an enlarged thyroid, and that the degree of thyrotoxicosis is not proportionate to the size of the gland.

In the classification, the age of occurrence, which essentially modifies the picture, and the presence or absence of tumefaction have been differentiated. Of fundamental consideration have been the hormonal signs of lobar activity, considering the lobes either singly or dually, in hyper- or hypo-activity, and in hetero-activity (that is, hyper-activity of one portion and hypo-activity of another).

TABLE III

CLASSIFICATION—DISORDERS OF THE PITUITARY GLAND

I. Anterior Lobe

A. Hypoactivity

- | | | |
|-------------------|---|---|
| 1. Preadolescent | } |Lorain-Levi Type |
| a. A-neoplastic | | |
| b. Neoplastic | } | { Amenorrhea, Dysmenorrhea, Metrorrhagia reacting to Anterior Lobe treatment. No signs of Posterior Lobe disorder |
| 2. Postadolescent | | |
| a. A-neoplastic | } | |
| b. Neoplastic | | |

B. Hyperactivity

- | | | |
|-------------------|---|--|
| 1. Preadolescent | } | { Gigantism (no signs of Posterior Lobe disorder) |
| a. A-neoplastic | | |
| b. Neoplastic | } | |
| 2. Postadolescent | | |
| a. A-neoplastic | } | { Acromegaly (no signs of Posterior Lobe disorder) |
| b. Neoplastic | | |

II. Posterior Lobe*

A. Hypoactivity

- | | | |
|-----------------------------|---|---|
| 1. Pars Intermedia (?)..... | } | { Polyuria (Bab) (Reaction to Pituitrin. Signs of Anterior Lobe and Pars Nervosa disorder absent) |
| 2. Pars Nervosa..... | | |

- | | |
|------------------------|---|
| B. Hyperactivity | { Hypophyseal Glycosuria (Increased metabolism, decreased sugar tolerance. Polyuria and signs of Anterior Lobe disorder absent) |
|------------------------|---|

III. Bilobar*

A. Anterior and Posterior Lobes

- | | | |
|------------------------|---|---|
| a. Hypoactivity | } | { Froelich's Type without, or with polyuria (Bledl) |
| b. Hyperactivity | | |
| c. Heteroactivity | } | { Gigantism or Acromegaly with increased metabolism and decreased sugar tolerance. Adiposity absent |
| | | |

- | | | |
|------------------------------|---|--|
| 1. Anterior Lobe hyperactive | } | { Gigantism or Acromegaly with Polyuria |
| Posterior Lobe hyperactive | | |
| 2. Anterior Lobe hypoactive | } | { Genital Aplasia, Nanism, Amenorrhea, etc., with Pituitary Glycosuria (Increased metabolism; decreased sugar tolerance) |
| Posterior Lobe hyperactive | | |

* (1) Pre- and (2) Post-adolescent varieties and (a) A-neoplastic and (b) Neoplastic types are subdivisions under each activity (Hypo- and Hyper-) as given under I, Anterior Lobe.

From this formulation of a temporary classification based upon what we believe to be a judicious selection of experimental evidence, we naturally proceed to a consideration of therapy. Therapeutic endeavor must not be haphazard, but rather directed along definite lines, such as those that a classification offers; and the clinical observation of therapeutic results along such lines will materially aid in the verification or negation of such a classification.

There has been much argument concerning the relative values of uniglandular and pluriglandular therapy. Upon the

basis of a cell selectivity, pluriglandular therapy has been advocated, and it is probably true that the body cell has to a degree the power of selecting from the blood stream certain of those elements essential to its maintenance. But the power of rejection is probably not of a corresponding degree of efficiency, as is well exemplified in the untoward effect produced by feeding thyroid or thyroid combinations to a patient whose thyroid function is normal or excessive. Again, from the standpoint of experimentation and rational advance in clinical observation, the author has felt that uniglandular therapy is the method of choice, realizing that pluriglandular syndromes may and do commonly exist requiring a combined therapy. This combined therapy, however, is based upon the clinical observation of the hormone signs representing the endocrine deficiency of two or more glands, and more valuable evidence may be acquired if first one gland is sufficiently tried and the clinical effects accurately noted, then the other, and then the combination of the two or more endocrine substances, corresponding to existing deficiencies.

As regards the standardization of pituitary material, we have little satisfactory information. There is no certainty that, even though the internal secretion exists in relatively large quantities in the fresh gland, it persists in the desiccated or chemically treated product. To use the fresh gland, of course, is not usually feasible, and uncertainty will exist until the active principle is isolated, synthesized, and accurately standardized. Considering the wide variability in the commercial products, a valuable point might be interpolated, and that is that the clinical observer should adopt a single preparation, and upon its effects base his therapeutic conclusions, for the present at least.

Another difficulty in the human being is the determination of the proper dosage. Anterior lobe has been prescribed by different workers in doses from 1 grain three times a day to 100 grains three times a day, with very little clinical evidence to guide the therapist; although the author considers that even small doses (for instance, 5 grains three times a day) have in a number of cases definitely intensified the headache associated with hyperpituitarism. As regards posterior lobe extracts, particularly when hypodermically administered, Engelbach and the author have suggested the "intestinal reaction" as a guide to

physiological tolerance (4). This intestinal reaction consists of a cramping, colicky sensation in the abdomen, succeeded within a few minutes by bowel evacuation, usually occurring five to fifteen minutes after the injection. The amount of pituitary extract (for example, pituitrin) required to produce this reaction varies widely in different individuals. At one time it was thought that in hypopituitarism the amount required to produce reaction might be considered as an index to the degree of deficiency, although clinical observation never fully verified this hypothesis. It may be said, however, that in many cases of frank hypopituitarism, it has required two or three times the dose of pituitrin to produce this reaction than in the normal individual. In regard to the oral administration of the posterior lobe substance, there is little to guide the clinician compared, for instance, to the manifold symptomatology resulting from the over-administration of thyroid extract. The intestinal reaction described as a result of the hypodermic injection of pituitrin has never been observed following the administration of the pituitary substance by mouth, nor have the vascular and general reactions. (Fully described in the reference above.)

Another source of general difficulty, particularly in the appreciation of therapeutic effects, is the great number of isolated clinical conditions that have been described as reacting or non-reacting to pituitary therapy, without the correlation of these symptoms with other pituitary signs or conforming them to definite classification. Among these conditions are tumor, headache, obesity, epilepsy, dysmenorrhea, amenorrhea, nervous and mental states, hibernation, diabetes insipidus, diabetes mellitus, adiposis dolorosa, shock, urinary incontinence, alopecia, onychia, ileus paralyticus, uterine inertia, decreased libido, sexual impotency, arterial hypotension, hyperthyroidism, asthma, orthodontal anomalies, and a variety of other conditions.

TUMOR

First, as regards tumor, especially when associated with hyperpituitarism, particularly acromegaly, the literature abounds with many successful procedures, including both the x-ray and radium.

X-ray and radium treatment. Schaefer (6) reports 8 cases of tumor of the hypophysis with acromegaly treated by this means, and accentuates the fact that the head should be so placed that the hypophysis is situated in the focus of the rays. Webster (7) reports a case of early acromegaly in which sixteen treatments were given with hard filtered rays through the temporal and frontotemporal areas, with good results. The first eleven were given at weekly intervals, then they were given fortnightly, and latterly at monthly and longer periods. The headaches were relieved, the "queer" feelings disappeared, the irritability and depression disappeared, and the optic discs returned to normal, while the fields for vision, especially for red, became greatly enlarged. Jaugeas (8) was successful in the use of x-ray treatments in tumors and hyperactivities of the hypophysis, stating that the change in the visual fields parallels the benefit and forms a gauge to the efficacy of treatment. Cavazzini-Bergamo (9) reports two cases of hypophyseal tumor with acromegaly which were greatly benefited by x-ray treatment by the Bécclère method—deep radiotherapy through the two temporal and frontal regions, at first every week, later less frequently.

Gramenga (10) treated a case by x-ray directly from the palate for an hour twice a month. The subject was forty-five years of age and had had amenorrhea for thirteen years. After eight treatments, the headache disappeared and the ophthalmoscopic signs became normal. The symptomatology returned later, however, and did not respond to treatment. Bécclère (11) reports a case of a giantess, aged sixteen; operation had been proposed for severe headache and visual trouble, but radiation weekly for ten weeks from the frontotemporal areas gave total relief from headache and improved the field of vision in the right eye in two months. Williams (12) reports a case of a woman, aged thirty-seven, with severe headache, nausea, dizziness, and vomiting, two months' diplopia, slight haziness of the optic papilla, and arteries which were very small. The headaches disappeared, and there was general improvement. Terrien (13) reports similar results. Favorable results of x-ray radiation in similar cases are reported by Kupperle (14), Gunsett (15), Cauvin (16), Calamet (17), and de Lapersonne and Cantonnet (18). Quick (19) reports three cases of *radium emanation*. In the first subject he imbedded five fine glass capillary tubes of radium emanation (unfiltered and a total strength of 15 millicuries) through trocar needles in the lower portion of the tumor and left them there. He attributes improvement in the headache, vertigo, and vision to the radiation, although some benefits may have been secured from previous operations, one the removal of an adenoma a year before, and a second for recurrence a month previous to emanation. Later, one tube of emanation, a total of 30 millicuries, filtered by 0.2 millimeter of aluminum and enclosed in a small rubber tube, was inserted in the space where the floor of the sella was removed and left for an hour and thirty minutes. A month later, two fine capillary tubes of emanation, a total of 3.2 millicuries, were imbedded through trocar needles in the same manner as the first treatment. At the time of writing, the condition had been definitely improved. The second patient, a woman of thirty-seven, during a pregnancy at the age of thirty, began to have attacks of vertigo, severe and persistent headache, impaired vision, and a cessation of menstrual function three years after the first symptoms were noted. Since the cessation of menstruation, there had been a persistent lactation. Gigantism and fat deposits were extreme. The sugar tolerance was very much increased. Under local anesthesia, a submucous resection of the nasal septum, back to the sphenoid, was done. The sphenoidal sinuses were opened, but the floor of the sella was not removed. A 0.2 millimeter aluminum tube,

containing 40 millicuries of radium emanation, encased in rubber, was introduced into the sinus, placed against the floor of the sella, and retained in position by gauze packing for twelve hours. After this there was definite relief of pressure symptoms, but the headaches again became more severe, although the vision continued to improve and the vertigo disappeared. About eight months later, 605 millicuries of radium emanation, filtered by 2 millimeters of lead and 0.5 millimeter of silver, were placed over the right temporal region, at a distance of 4 centimeters from the skin, left in place for five hours, and repeated the following day over the left temporal region. After this there was a lessening of the headache, but it did not disappear. The vision improved appreciably and lactation ceased. The third subject died of meningitis a month following treatment, so that no report was possible.

Bertolotti reports a number of cases treated by x-ray and radium, with notable improvement in several. He feels that the best results are obtained in early cases. Ranschburg (20) reports two cases of dystrophia adiposogenitalis with tumor treated by x-ray, the first subject presenting headache, fainting giddiness, loss of vision, increasing papillitis, and weakness. The skull was divided into eight sections and treated with Roentgen ray. In the course of four weeks, eight treatments of thirty to forty minutes each were given, followed by twenty minutes of treatment through the hard palate. At the end of six months, the symptoms of tumor, except those due to destruction, had disappeared, while, in spite of treatment with organ extracts, there had been no change in the signs of dysfunction caused by the probable total destruction of the hypophysis. The second subject, a young woman at the age of twenty-one, weighed between 80 and 90 kgm., increasing within a few years to as much as 115. There was an abnormally large and deep sella turcica; tumor was suspected. After ten days of Roentgen ray treatment the patient was able to distinguish light from darkness. A short time later, the vision increased to about half normal, and the facial paralysis was cured. There was no effect upon the impairment of smell and taste, nor upon the growth of hair.

Ascoli and Faginoli (21) suggest an interesting phase of the subject, namely, the stimulation of a deficient pituitary by means of deep radiation with the x-ray, whereas all previous attempts have been directed to the destruction of tissue. The first case was one of dystrophia adiposogenitalis, without demonstrable tumor; the subject had received several months' pituitrin and endospermin treatment, with but slight improvement. He had four radiations of the hypophysis at intervals of one month. At each sitting, three different fields were radiated, one frontal and two temporal, for thirty-six minutes in all, at a distance of 45 cm., using an aluminum filter of 2 mm., S. Et. 18-20 cm. and M. A., 3.5. Twenty-five days after the first irradiation, pubic hair began to grow, the penis and testes increased in size, erections became frequent and complete, and there was increased sexual tendency. The height increased 5 cm., and the fat tended to diminish, the chest measurement dropping from 86 to 81 cm. The second, a patient with scleroderma who had not responded to other treatment, received radiations over both the hypophysis and the thyroid, with signs of some improvement. Other cases showed failures or varying degrees of improvement. Fraenkel (22) also expresses a belief that the stimulating action of slight irradiation may prove successful in endocrine function.

Surgical treatment. Concerning the surgical treatment of pituitary tumors, little need be said. Quick (19) in his review of the literature, emphasizes the wide variation in operative mortality and

the relatively small group of cases in which surgery offers anything worth while. Kanavel (23) places the operative mortality in the neighborhood of 35 per cent in the hands of those doing little cranial surgery, but mentions the work of Hirsch (24) and Cushing, where the rate is down near 10 per cent. In his own series of 15 cases, there were 4 deaths. Cushing (1) reports of 43 cases, a total of 61 operations, 10 per cent. (The technique is now probably improved.) Moritz (25) states that the visual disturbance and headaches are relieved by surgery, while the metabolic and trophic changes may be altered but slightly, or not at all. A consideration of the various operative procedures and the relative merits of the same cannot be considered in this article.

HEADACHE

Pardee (26), from a review of the literature and a consideration of 7 cases, concludes that pituitary disturbance constitutes a fairly common cause of headache, usually located between the temples, deep in behind the eyes, and associated with dyspituitary signs. He believes that the sella turcica in most cases shows demonstrable abnormalities. In a large percentage of these cases, the headaches and accompanying symptoms disappeared upon the administration of the whole pituitary gland substance, in doses from .25 grain to 2 grains three times a day. He also accentuates the fact that these headaches may be physiological, occurring during the menses and pregnancy.

Blumgarten (27) states that pituitary headaches are distinctive, that the patients all show characteristic markings, such as a broad forehead, with prominent supraorbital regions, overlapping teeth, changes in the secondary sex characteristics, amenorrhea, impotency, sterility, or a pituitary psychology (e. g., males having feminine psychology). The basis for the treatment of the headache, he feels, is the fact that physiological hypertrophy of the pituitary gland in a small sella turcica is the cause, and that injection or feeding of pituitary extract removes the need for hypertrophy. Blumgarten found no success with placenta and corpus luteum in many subjects whose headaches yielded to pituitary extract.

Timme (3) calls attention to the association of migraine with other signs of pituitary disturbance, particularly the association with the menses, believing that at this time the pituitary body enlarges. He feels that the sella turcica of a person subjected to these disturbing factors is too small to accommodate the enlarging gland, and pressure against the surrounding structure of the hypophysis occurs, producing first erosion of the sella, and then pressure against the softer structures beyond, such pressure occasioning headache. He narrates post-mortem confirmation of unilateral pressure exerted by an enlarged hypophysis upon the cavernous sinus, in a case of migraine, by Deyl, at Paris; the work was later confirmed by Plavec. He also feels that the phenomenon of epilepsy may be upon a similar basis, a periodic enlargement of the hypophysis in a sella not sufficiently large to accommodate it, causing the critical moment, thus precipitating an attack, and from this standpoint attaches some importance to the frequently recognized association of epilepsy and migraine.

Glassburg (28) presents a case of pituitarism in which the bi-temporal headache, muscular fatigue, etc., were probably relieved by pituitary extract, 4 to 8 grains a day by mouth. Cushing (1) felt that the headaches associated with pituitarism, usually bitemporal, often severe and persistent when there is considerable glandular hypertrophy, are presumably due to the distention of the glandular

envelope, and noted that they often subsided, and coincidentally presumably, with a stationary process or with a full distention of the dural capsule and widening of the sella. He felt that splitting of the tense capsule of the gland in two cases produced relief.

Engelbach and Tierney (4) used the term *pituitary headache* as not referring to the type of headache caused by neoplasm of the pituitary or other brain tumor, for the reason that the headache is found present in many cases free from evidence of enlargement of the sella turcica or other signs of intracranial pressure. Its frequent occurrence in diseases of the pituitary is sufficient reason for the term, and will stimulate closer observation of hormonal signs and symptoms in every case of persistent recurring headache, particularly those which are associated with menstrual disturbance. The association of migraine with general pituitary signs, its association with the menses, its frequent cessation at the menopause, and the fact that in the author's experience many cases of migraine have been definitely benefited by pituitary therapy, suggest the more than casual relationship between the complex migraine and pituitary disturbance.

OBESITY

The author has felt that the characteristic obesity of hypopituitarism represents deficiency of the posterior lobe, although Beck (29) believes that the development of obesity is due to an anterior lobe deficiency, and has found definite changes in the deposition of obesity under anterior pituitary lobe therapy (2.5 grains two or three times a day) and thyroid from 0.5 to 1 grain two or three times a day. The author feels that the loss of weight is not an adequate criterion for the effect of treatment, but that the redistribution of fat and reductions in the characteristic areas of increase are of more significance. Unfortunately, in these cases no adequate conclusion can be drawn, because of the fact that thyroid was used in conjunction with the anterior lobe pituitary substance.

Von Dziembowski (30), in a case of *dystrophia adiposogenitalis*, examined microscopically a small piece of the biceps. The picture showed a few muscular fibers, and these atrophic, with an enormous increase of fatty tissue. In this case, treatment with thyroid, adrenal, and testicle was unsuccessful; but injections of an ampule of hypophysin were tried, with splendid success. The patient lost weight, libido returned, and the muscles became thinned, with an increased tonus. Most of the author's cases have been combinations of genital hypoplasia and obesity of the ordinary Froehlich type; or that occurring after adolescence, consisting of obesity of the characteristic type and genital disturbance, as manifested by amenorrhea, loss of libido sexualis, etc. These cases have been treated largely by a combination of both the anterior and the posterior lobe substances by mouth, and antuitrin and pituitrin hypodermically injected, some showing definite response, as will be noted in type cases. In other cases, thyroid has been combined; and a most important point must be here accentuated, that is, that cases have been seen in which thyroid would produce response only to a certain degree. When this was stopped, and pituitary substance substituted, response might

be again noted to a certain degree; but the optimum response in many of these cases, and the response much greater than that secured by either thyroid or pituitary substance alone, was secured by the combination of these two substances. Timme has called attention to the fact that very small doses of thyroid (1/100 or 1/10 grain every day, or on alternate days) will frequently enhance the effect of pituitary administration.

EPILEPSY

Lowenstein (31) reports 16 cases of epilepsy studied from the standpoint of possible endocrine disturbance, particularly hypophyseal. Five cases, or 31 per cent, showed one or more features possibly to be ascribed to pituitary change. In 8 cases, or 50 per cent, roentgenographic examination showed changes in the sella. In this series, 5 cases were apparently benefited by pituitary gland administration, the preferable product seeming to be extract of the whole gland, and the most satisfactory method of treatment, hypodermic injections. No improvement was shown in cases showing typical epileptic constitution, nor in cases with abnormalities of the fundi or visual fields. Other physical signs referable to the hypophysis, such as sella turcica changes, and variations in weight or height, offered no criteria to judge success or failure.

Engelbach and Tierney (4) report 6 cases of epilepsy associated with definite signs of pituitary deficiency: 4 male, 3 of which appeared to be pure anterior lobe insufficiency, and 1 bilobar; 2 female, both of which showed hormonal signs of insufficiency of both lobes. Three cases were under observation for a considerable period of time, 2 showing definite benefit from pituitary treatment. The other 3 subjects were not under observation for a sufficient length of time to appreciate clinical results. Numerous other isolated cases have been reported in the literature, many with apparently successful response. Tucker (32), in a study of 200 subjects, 63 (or 31.5 per cent) of whom revealed some evidence of pituitary disturbance, feels that there is a definite relation between the undersecretion of the pituitary gland and a group of periodic convulsive attacks, usually termed epilepsy, but that this group is divided into a chronic hypopituitary type and a transitional hypopituitary type, by both clinical and roentgenographic evidence; pituitary gland feeding has a markedly beneficial effect, not infrequently leading to cure.

NERVOUS AND MENTAL STATES

Many peculiar nervous and mental phenomena have been described as associated with pituitary disturbance. Fliess (33) describes a complex nearly always observed in women after pregnancy, or in women with diseases of the ovaries, consisting of obstinate neuralgias (sciatica, occipital neuralgia), extreme weariness, psychic disturbances (diminished concentration of thought), polydipsia, polyuria, and enuresis, reacting favorably to pituitary preparations. Weygandt (34) feels that two psychic symptoms have not been fully appreciated in association with hypophyseal obesity: (1) feeble-mindedness, and (2) a cheerful disposition, with psychomotor unrest. The findings are not uniform, but reveal certain general factors, especially feeble-mindedness of more or less severe grade up to the severest dementia of idiocy, frequently in combination with a cheerful, amiable disposition and a tendency to joking and harmless, irritable, restless behavior. There are also individual patients with more than average intelligence and earnest, almost depressive habitus. The author accentuates the first type, although our experience cer-

tainly has shown the preponderance of the group showing an intelligence either normal or above normal, with the earnest and at times depressive habitus. Tucker (32) described a number of pituitary psychoses peculiar to adolescence, separating them into four groups, giving the roentgenographic findings of the sella turcica and the psychoses associated with both the hyper- and the hypo-active types. He concludes that in these various psychoses of pituitary origin, in many cases showing decreased pituitary secretion, the response to pituitary feeding was prompt and satisfactory.

The author has noted as a most constant association with pituitary disease, a marked mental disturbance. The main features have been nervous instability, irritability, failure of concentration, dissociation of ideas, memory defects, inconstancy, temperamentalism, occasional brainstorms, emotionalism, wanderlust, and a variety of other psychic manifestations. Physical complaints have shown frequent paresthesias, varying from tingling to definite formication. These symptoms frequently respond early to proper substitutional therapy—long before there are definite responses in the objective sphere.

GLYCOSURIA

Although the pancreas has received fundamental consideration in the etiology of diabetes mellitus, there are many authors who feel that other endocrine organs, such as the adrenals, thyroid, or hypophysis, may be factors in the production of glycosuria. Borchardt (35) found that injections of the whole gland caused glycosuria in rabbits. Franchini (36) could not confirm this, although Cushing (1) reported similar results. The association of acromegaly with glycosuria has been frequently noted in the literature (Borchardt, Falta (37), Schlesinger (38), Cushing (1), Frankl-Hochwart (39), and others), and there are a number of reports of acromegalic and diabetic subjects dying in coma. Many have felt that the association of diabetes with pituitary disease was due to secondary disease in the pancreas, which contention apparently has been verified by some observers, but careful post-mortem examination in other cases of acromegaly and diabetes showed no pathological change whatsoever in the pancreas. Koopman (40) reports two cases of diabetes mellitus apparently definitely benefited by the administration of hypophysis tablets, and cites another case reported by Steensma (41) of a young girl showing some tendency to adiposity, with an enlarged sella turcica and glycosuria, who responded successfully to hypophysis substance. Koopman draws the conclusion that, although he is aware that proof is lacking that these cases are hypophyseal diabetes, from the therapeutic results it is probable that the hypophysis had played an important part.

Engelbach and the author, in a series of 711 pituitary cases (including pluriglandular disorders with pituitary involvement), found 8 cases of glycosuria, 3 of which have been reported in Tice's Practice of Medicine. All of these cases except one failed to respond to pituitary therapy, although it is felt theoretically

that those cases associated with hyperpituitarism, such as acromegaly, should be definitely treated along such lines as x-ray or radium directed to the pituitary. Glycosuria has been frequently noted early in the case of acromegaly, later disappearing. This disappearance may coincide with the transition of hyper- to hypo-activity, which so frequently occurs, and should be, as in other cases of hypopituitarism, an indication of intensive pituitary therapy, both by feeding and hypodermic administration.

DIABETES INSIPIDUS

There is an extensive literature concerning the rôle of the hypophysis in the production of diabetes insipidus. Earlier workers [Talqvist (42), Meyer (43), Seiler (44), Socin (45)] thought the condition due to lack of the kidneys to secrete concentrated urine. Finkelberg (46), Schwenkenbecher (47), Falta (37), and Forschbach and Weber (48) did not believe that the concentrating power of the kidney was lost, but that there was a pathological stimulation which produced larger amounts. Spaether (49) considered diabetes insipidus to be a paresis of the renal vasomotor nerves, of either central or peripheral origin, and Ebstein (50) believed that the condition was due to a primary polydipsia, with a resultant polyuria. Bernard (51), in 1849, proved that by puncturing the medulla oblongata and the brain stem in various places, definite polyuria would occur. In 1870, Eckhard (52), produced polyuria by various types of irritation of the vermiform process of the middle lobe, and injury to the posterior lobe of the brain. Kahler (53), in 1886, produced permanent polyuria and polydipsia in animals by injecting small quantities of concentrated silver nitrate solution into various portions of the brain.

The hypophysis began to receive attention after Schafer demonstrated that the administration of posterior lobe extract produced polyuria. This work was confirmed by Schafer and Oliver (54), Magnus and Schafer (55), and Schafer and Herring (56). Later, Pentimalli and Quercia (57), van den Velden (58), and Motzfeldt (59) found divergent results. The previous theories of hypersecretion of the pituitary as a factor in polyuria, began to swing toward the theory of hyposecretion. Bab (60) believed diabetes insipidus to be due to hypofunction of the *pars intermedia*, or a disturbance of the reception of the secretion in the *pars posterior*, or a propagation of the secretion in the cerebral *lecunae*. Biedl (61) noticed many clinical discrepancies, such as the association of diabetes insipidus with *dystrophia adiposogenitalis*. The same association has been noted by Fearnside (62), Marañón and Pintos (63), and Schuenemann (64). The pathology in the literature is full of contradictory results. Houssay (65), believes it to be due to injury to the neighborhood tissue; Leschke (66), to lesions in the midbrain, especially the *tuber cinereum*. Claude and Lhermitte (67), and Olacchia (68) have reported cases in which only the *infundibulum* was involved. Most of the literature, however, is concerned with the response of the syndrome to the administration of the posterior lobe extract, and many striking results are recorded. Of course, it must be remembered, as has been frequently stated, that the results from the admin-

istration of the posterior lobe extracts do not positively prove the pituitary origin of diabetes insipidus, but they certainly are suggestive.

Engelbach and the author have observed 15 cases, 11 of which were reported in 1920 (4). Of these, 5 had no definite osseous, adipose, or general changes, or other hormonal signs that would relate them specifically to pituitary disorder. On the other hand, 6 had very striking pituitary signs other than polyuria and nervous manifestations. In 5 of these subjects, posterior lobe extract (puitritin) exerted a decided influence upon the polyuria and other symptomatology. In 4 cases, including 2 tumors, puitritin was not instituted. In 1 case, showing what we deemed to be an associated disorder of the anterior lobe, tending to gigantism, there was absolutely no response to puitritin treatment. Another case, however, of similar makeup, did respond. In all cases it was necessary to continue the treatment indefinitely, and in only one case, after the condition had been controlled by subcutaneous treatment, was the patient able to continue on pituitary treatment by mouth (in the dosage of 10 grains three times a day), without a return of the symptomatology. However, if the oral administration was discontinued, there was a prompt return of the polyuria.

Most cases reported in the literature have failed to respond to the oral administration, although a few isolated cases have been observed responding to pituitary substance which had been salol-coated, possibly preventing some destructive chemical transformation in the stomach. Rees and Olmsted (69) were able to control a case of diabetes insipidus as effectively with salol-coated capsules of the desiccated posterior lobe, as with hypodermic extract.

In the author's recent series of cases, there has been one of more than passing attention, and that is the association of marked diabetes insipidus with sphenoidal sinusitis. At the present time, the sphenoidal condition has been practically cleared, but the polyuria persists, requiring 2 cc. of puitritin (0) daily for control.

SMOOTH MUSCLE TONE

The use of puitritin in many conditions with a fundamental loss of smooth muscle tone, has been successful. Mikhailoff (70) reports the successful use of puitritin in the treatment of urinary incontinence, reporting 19 cases, all successfully treated, and stating that

four injections are sufficient to cure the condition. Bandler (71) accentuates the value of pituitrin in post-operative tympanites, and in the stimulation of intestinal peristalsis. Its clinical value in paralytic ileus is well known, and its successful use in uterine inertia and in obstetrics is so well accepted that comment is unnecessary, except to mention the apparently growing objection of many obstetricians to its routine use.

SEX DISORDERS

Hoffstätter (72) reports good results from the administration of pituitary preparations in cases of amenorrhea accompanied by uterine and ovarian hypoplasia. The author has found amenorrhea rather constantly associated with deficiency of the anterior lobe, associated with infantilism and genital hypoplasia in the preadolescent deficiency, and amenorrhea, with decreased libido sexualis, in the post-adolescent deficiency of the anterior lobe. In some of these patients there was definite response to anterior lobe substitution alone, whereas in others absolutely no response was shown. Dysmenorrhea and menorrhagia are more questionable in their association with pure pituitary disease; although clinical responses in our own hands to this line of therapy have warranted more prolonged and careful clinical investigation along this line, with particular attention to the association of these symptoms with other pituitary signs, and to conformity of the afflicted individuals to definite types, as suggested in our classification. Concerning the psychological phase, such as frigidity, decreased libido, and impotency, there is no question about the frequent association with pituitary deficiency, and experience has shown numerous responses of these particular conditions to pituitary substance administered hypodermically and by mouth, especially the anterior lobe preparations. In certain cases, types of which will be shown, there has been a definite stimulation of the genitalia, including marked growth of the testes and penis, attributed to anterior lobe substitution alone.

BLOOD PRESSURE

The association of endocrine dyscrasia with hypertension has received considerable attention; Engelbach's (5) analysis of 500 endocrine cases showed that 46, or 10 per cent, had a blood pressure above 160, all cases in which a diagnosis of nephritis or arteriosclerosis was suspected having been excluded. Of these, 30 per cent showed pluri-glandular deficiency, and it was impossible to determine the dominating influence. A combination of pituitary and thyroid deficiency was exhibited by 26 per cent; 25 per cent were associated with the menopause; 11 per cent showed hormonal evidence of only pure pituitary disturbance, 4 with deficiency, and 1 with hypersecretion. This association is of interest, especially considering the fact that, contrary to the bulk of animal experimentation, our experience has shown that almost 50 per cent of the subjects show an immediate and direct depressor action following the subcutaneous injection of 15 minims of pituitrin (0), this reduction in blood pressure varying from 10 to 30 mm. of mercury.

GLAND THERAPY

The treatment of other endocrine diseases based upon reciprocal relationship has received considerable attention, particularly hyperthyroidism. Hoffstätter (72) found marked improve-

ment in 15 cases of Basedow's disease following repeated injections of 1 cc. of posterior lobe extract, followed for a time by the oral administration of desiccated pituitary substance. He concludes that the anatomical changes in the thyroid after hypophyseal therapy indicate an influence of the thyroid, in the sense of an inhibition of secretion with respect to the pituitary. Many other observers have reported varying effects. The author's experience has been decidedly unsatisfactory.

A variety of other conditions have been reported as associated with pituitary disturbance, and variable results recorded. Eye conditions have been especially prominent, particularly the response of various hemianopsias, retinitis pigmentosa, etc. In general, it may be deduced, from a review of the tremendous literature that has accumulated, that the pituitary plays a rôle in many of the above conditions, and that the recorded responses to substitutional therapy cannot be dismissed as purely coincidental; although one must appreciate the tremendous value of experimental physiology in placing the entire subject upon a sound basis and realizing that experimentation to date offers a variety of conflicting evidence. It must be remembered that laboratory subjects, from tadpoles to dogs, are essentially different from the genus homo, and that from careful, well controlled, correlated clinical observation, our most valuable, pertinent, and applicable information is to be secured. One cannot help noting that in the literature generally an isolated syndrome is selected and discussed, particularly with regard to therapeutic response, without suitable correlation with other hormonal signs, both physical and mental, or with chemical and metabolic observations. For this reason, it is difficult to draw conclusions, either favorable or unfavorable. This lack of correlation and conformity leads us to accentuate the value of a classification, based upon what appears to be the most acceptable experimental and clinical evidence, as a means of furthering our investigations along definite lines and enabling us to evaluate more correctly therapeutic response. We may eventually come to feel that the pituitary is a glandular entity, with no particular distinction to be made between its component lobes (as Bell is inclined to believe); but we feel that investigation along the lines of separated function will enable us more quickly to reach that conclusion, provided it be the true one. Or, on the other hand, if

the gland is physiologically dualistic, investigation along the lines of such a classification will enable us more quickly to confirm or to reject.

Another point that has not been sufficiently emphasized, and which should have particular appeal to the pediatrician, is the early recognition and treatment of pituitary disorders, Harvey (73) called attention to the desirability of early diagnosis of endocrine deficiency, and the greater amenability to treatment in that stage. Our experience has fully verified and accentuates this point. Our most decided therapeutic results (for instance, in pituitary obesity) have occurred in the earlier years of life. The earlier the disorder has been recognized and treatment instituted, the more effective and decided has been the reaction. In those cases in which it has been possible to institute treatment a few months after the disorder became evident, remarkable responses were achieved.

Another and most perplexing consideration, taking into account the tremendous number of possible combinations, is the reciprocal involvement of other glands. Because of this intricate reciprocal relationship, there has been given full play of diagnostic fancy in the realm of pluriglandular syndromes. We feel that each gland has a definite system of characteristic hormonal effects and signs, and with proper clinical investigation of the many pluriglandular syndromes, the glands affected may be determined, and frequently the gland which is physiologically preponderating. There is no doubt that theoretically there are probably always minor reciprocal effects in all endocrine disturbances, but practically we believe that we see uniglandular syndromes, - g., frank hyper- or hypo-thyroidism, presenting characteristic and distinctive symptoms. Another point for consideration is the probability that one gland is fundamentally at fault and others show a secondary disturbance, and that therapy directed to the primary glandular imbalance may automatically correct the reciprocal involvement. We have also found that many of the pituitary insufficiencies have been in their earlier stages apparently uniglandular, and that after a variable length of time, usually a year, there almost constantly occurs a secondary reciprocal involvement of the thyroid or of the gonads. We have found also that, after this reciprocal involvement, the diagnosis of which is based upon the associated hormonal signs, there

is less likelihood of successful response to therapy, either singly or combined. We have found the most constant reciprocal relationship to be a combined deficiency of the pituitary and the thyroid, and that, whereas these subjects will respond to a degree to thyroid therapy alone or to pituitary therapy alone, the optimum response is invariably secured by a combination of the two.

Another point that needs definite accentuation, and one insisted upon particularly by Pottenger (74), is the remarkable association of endocrine disturbance with the sympathetic nervous system; and to this secondary sympathetic nervous system response, we must look for the explanation of many of our clinical symptoms, vasomotor responses, muscular phenomena, reflex changes, etc.

It is deemed advisable to demonstrate a few cases exemplifying what we feel to be the salient features of the classification, followed by a number of cases showing harmonic responses to therapy.

CASE I. MISS M. L., GEN. NO. 727, AGED 18, CLERK*

Chief complaints. The patient complained of amenorrhea (having had no period at the age of 21 years). Weight at birth was normal. The first tooth erupted at six months, and all deciduous teeth were present at the end of the second year. The patient walked not later than the thirteenth month, and was talking well at the age of one and one-half years. Mentality during childhood and early adolescence was rather above normal. No adiposity or localized puffiness of the hands, feet, etc., was noted at any time. No changes occurred in the skin or appendages (including perspiration). There have been no particular gastrointestinal or nervous disturbances. No development of primary or secondary sex characters has occurred, and no increase in growth since the age of thirteen or fourteen.

Past history. The patient had had measles, possible typhoid at the age of fourteen and frequent tonsillitis, followed by otitis media. There was nothing noteworthy in her *personal* and *family history*.

Physical examination. The patient was 78 lbs. in weight and 4 ft. 4 in. (132 cm.) in height. From vertex to symphysis she measured 27 in. (68.25 cm.); from symphysis to soles of feet, 25 in. (63.25 cm.). The span was 56 in. (142 cm.). The hand, "en petite," was of typical hypopituitary type (one-third smaller than normal), without clubbing or tapering of fingers. The head was rather large in proportion to the rest of the body; it was 20½ in. (52 cm.) in circumference; the superior maxilla measured 16¼ in. (41 cm.); the inferior maxilla at the tip of chin, 15¼ in. (39 cm.). The circumference at the navel was 25 in. (63.25 cm.); at the hips, midway between trochanters, 29¼ in. (74 cm.); at the middle of the thigh, 13¾ in. (34.75 cm.); and of the leg, 10 in. (25.25 cm.). There was complete absence of secondary sex characters, very slight lanugo on the mons veneris, absolutely no hair in the axillæ or on the face. The breasts were not

*Reported in full in Med. Clin. N. Am., St. Louis number, Nov., 1920 (Endocrine Amenorrhea, Wm. Engelbach.)

developed. The face was typically infantile. The hairline was rather low, the eyebrows very thin; the nose was slightly retrousse; no adiposity was present. The pulse was slow, but otherwise normal; the blood pressure was 124/90. The profile showed slight recession of the chin; the mouth showed recession of the lower jaw, with poor occlusion of the anterior teeth; the *upper incisors were very large, lateral canines very small*; all permanent teeth were present except the posterior molars. Both lobes and isthmus of the thyroid were slightly full.

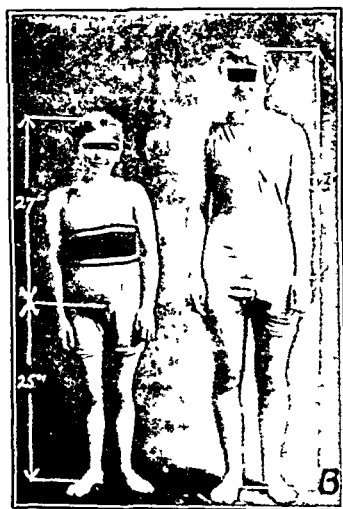
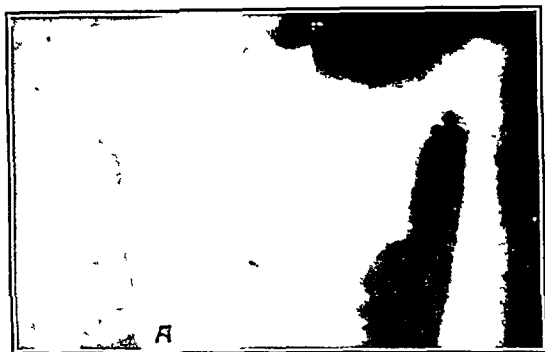


Fig 1. (A) Note the infantile, virgin type of breast development. (B) Case I, age 19. Note the general infantilism, fecies, and underdevelopment of the osseous system compared with the normal girl of corresponding age. (C) Infantile vulva; absence of secondary sex characters

The *urine* was negative, except for a slight trace of albumin. The *blood*, including Wassermann test, was normal. *Carbohydrate tolerance* was increased; blood sugar the first hour tested 0.180%; the second hour, 0.120%. The *basal metabolism* was 0.108%.

Radioscopy showed a normal sella turcica, and epiphyseal lines clearly evident in the head of the radius and in all metacarpals and phalanges. Complete ossification had taken place in carpal bones; the phalanges were free from tufting or mushrooming; the bones were slender.

The above case is believed to correspond to the Lorain-Levi type of hypopituitarism, and, according to our classification, represents a pure anterior lobe deficiency of the preadolescent type, evidencing marked osseous underdevelopment and a decided genital hypoplasia, with amenorrhea. The patient was first seen in 1919 and remained intermittently under treatment for practically a year. The treatment consisted entirely of anterior lobe substitution: gland substance by mouth, 10 grains, three times a day; and "Antuitrin" hypodermically, from 5 minims to a dosage as high as 2 cc. daily. There was no response in the development of the primary or secondary sex characters, no production of menstrual periods, and only a slight increase in growth, despite the fact that skiagraphic evidence disclosed open epiphyses and suggested the possibility of growth.

A perusal of the literature and personal communication with Dr. H. Lissner, of San Francisco, who has observed and treated a number of similar cases, bring out the fact that the preadolescent type of anterior lobe hypopituitarism does not readily respond to treatment, especially when seen and treated after the condition has been long established. On the other hand, in our experience, cases of anterior lobe deficiency occurring after puberty and manifest by such symptoms as amenorrhea, loss of libido sexualis, decreased muscle tone, etc., have responded much more satisfactorily to substitutional therapy, that is, anterior lobe substance by mouth, 5 to 10 grains, three times a day, and "Antuitrin" hypodermically, 1 to 2 cc. daily.

CASE II. MISS K. S., GEN. NO. 2237, AGED 18. REFERRED BY
DR. H. C. RUDDICK, EVANSVILLE, IND.

Chief complaints. The subject had complete amenorrhea. She often complained of severe, dull temporal headaches, radiating directly inward, at times associated with unconsciousness and convulsions. There had been a noticeable gain in weight (over 20 lbs. during the past three years), particularly distributed about the girdle and bust, with increased deposition in the supraclavicular areas, on the backs of the hands, and about the ankles. The hair was increased in dryness, and tended to fall out. There were no marked changes in the nails or teeth. There was increased nervousness, irritability, and fatigability. Cardiac palpitation and slight dyspnea were noted after exertion. Pigmentary changes were manifest, transient in

character and usually associated with the headaches. Constipation was complained of, and nocturnal insomnia without somnolence.

Course. The syndrome dated back to puberty. The first menstruation occurred at the age of 15, was normal and four days in duration; the second period was one month later, since which time there has been complete amenorrhea. All other complaints dated to this time. Chief among them was the headache, extremely severe, frequently requiring morphine for relief, dull, boring in character, temporal, radiating directly inward, without retro-ocular or mid-frontal localization, and unilateral. At times it was associated with unconsciousness and convulsions of tetanic character. They have occurred regularly once or twice a week, for the past three years, never associated with visual disturbance, scotomata, nausea, or vomiting. Coincident with occurrence of headache, there was a gain in weight of about 20 lbs., particularly about the girdle and breasts; also increased deposition in the supraclavicular areas and on the backs of the hands, and a suggestion of cuffing about the ankles. The hair showed increased dryness and tendency to loss. There were no other dermal changes, except transient chloasma pigmentation, usually associated with headache. There has been an increase in general nervousness, irritability, apprehension and restlessness, cardiac palpitation, and constipation. There have been no polyuria, polydipsia, polyphagia, nor change in the visual field. The patient had received hypodermic injections twice weekly for a number of months (probably a corpus luteum preparation), without relief. Dilatation of the cervix and curettage were performed, and douche and tamponade treatment given, without avail. Two months preceding our observation, the patient received Burroughs, Welcome & Company's "Mixed Glands No. 2." This caused slight loss of weight, but no other change.

Past history. The patient had measles at the age of twelve. Personal and family history were negative.

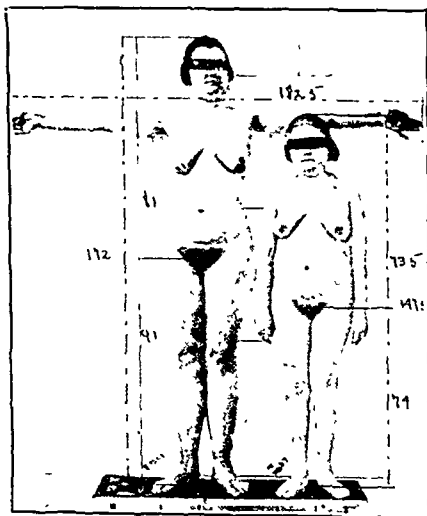


Fig. 2. Case II, age 18. Amenorrhea, associated with underdevelopment of the osseous system, representing anterior lobe deficiency. Note the suggestion of posterior lobe deficiency in the characteristic obesity. This subject is compared with a normal girl of corresponding age.

Physical examination. The patient was abnormally small (see comparison of figure with normal). She was 112 lbs. in weight and 4 ft. 10½ in. (148.5 cm.) in height. From symphysis to soles of the feet she measured 29½ in. (74.75 cm.), and from symphysis to vertex, 29 in. (73.5 cm.). She was of a general pituitary type, with slight tendency to obesity, fullness about the lower abdomen and padding on the lateral aspects of the thighs. The skin was slightly dry. The hands were classically small, with short fingers and slight padding on the dorsa. *Head.* There was a faint brownish pigmentation about the forehead; the ears, eyes, nose and mouth were normal. The chest, heart, abdomen, genitalia and reflexes were normal also.

The urine was negative, except for two or three leucocytes per high power field (non-catheterized specimen). The blood, including Wassermann test, was normal. *Sugar tolerance.* The blood-sugar, after a fifteen-hour fast, tested 0.065%; one hour later, following 1.59 gm. dextrose per kg. of body weight, 0.112%; two hours after dextrose, 0.113%. The basal metabolic rate was —25%.

Pituitrin test:—

	Blood Pressure	Pulse	Temperature	Respiration
	118/70	80	98	18
9:40—Pituitrin (0) m. xv. subcutaneously.				
9:45—	118/75	82		
9:50—	120/85	80		
9:55—	115/85	82		
10:00—	118/80	80	98	20

Pallor during test, no abdominal or other disturbances.

Adrenalin test:—

	Blood Pressure	Pulse	Temperature	Respiration
	115/80	80	98	20
11:35—Adrenalin Chloride (1:1000) m. vii. subcutaneously.				
11:40—	118/75	86		
11:45—	118/80	84		
11:50—	115/80	84		
11:55—	112/75	80		
12:00—	115/75	80		
12:05—	113/70	90		
12:10—	118/75	90		
12:15—	118/75	88	98.2	18

During test, nervousness and tremor.

A skiagram of the carpal bones showed normal ossification; epiphyses about the wrist were not united. A skiagram of the skull showed a small sella turcica, well defined, without excavation or erosion.

Report of ocular examination (Dr. B. D. Ravdin, of Evansville, Indiana): No impairment of vision was observed, no intraocular nor optic nerve alterations, no scotomata, no enlargement of the blind spot of Marriott, but there was slight alteration in the visual fields for form and color, showing slight contraction of the temporal fields from above downward and slight contraction below; this was present in both eyes (however, the observer did not construe it to be a typical or true bitemporal hemianopsia).

This case exemplifies, we believe, a deficiency of the anterior pituitary lobe, manifest by underdevelopment of the skeletal system, amenorrhea, etc. The obesity occurring coincidentally suggests posterior lobe involvement. The headaches are possibly pituitary, and there unquestionably is a secondary thyroid defi-

ciency, as noted in the dermal changes and the low basal metabolic rate. The following treatment was recommended: (1) anterior lobe pituitary substance, $2\frac{1}{2}$ grains and pituitary substance, entire gland (Parke, Davis & Co.), $7\frac{1}{2}$ grains, three times a day; (2) thyroid gland substance, beginning with $\frac{1}{4}$ grain, three times a day and increasing to tolerance; (3) "antuitrin," 1 cc. hypodermically two or three times a week; and (4) "Pituitrin (0)" hypodermically two or three times weekly, beginning with a dosage of 5 minims and increasing to tolerance; the index to tolerance was the so-called "intestinal reaction," consisting of abdominal cramping and desire for defecation, occurring fifteen or twenty minutes after the hypodermic injection. This treatment was persisted in for a period of six months, and then the patient, because of her improved condition, ceased to report to her physician. A report received a year later states that the headaches were not so severe nor so frequent, morphine having been required on but one occasion, at which time the necessity was questionable. The weight had decreased 10 lbs. *The menstrual periods had become perfectly regular*, of the twenty-eight-day type, four to five days in duration, with no pelvic pain, but usually associated with frontal headache of eight or ten hours' duration, during the first day.

CASE III. P. B. M., GEN. NO. 1438, MALE, AGED 15. REFERRED BY
DR. NEIL MOORE, ST. LOUIS

History. The patient was normal at birth. Dentition occurred normally, and locomotion and speech were not remarkable. Development was normal until the age of seven, at which time, following a mild attack of measles, the patient began to gain weight rapidly, reaching 105 lbs. at the age of ten and 175 lbs. at the age of fourteen; the existing weight was 205 lbs. The increased adipose tissue was distributed particularly about the upper thighs and abdomen. The patient complained of occasional headache and of being markedly drowsy and sleepy during the day. He perspired easily, and stated that his hair grows very rapidly. Other symptoms were indefinite visual disturbance, increased thirst, without polyuria, and some tendency to constipation. The mentality was normal for the age, without tendency to decreased cerebration. Diffuse superficial tenderness existed over the entire body. *Past history.* The patient had measles at the age of seven (to which he dates the adiposity) and later, questionable malaria. The *personal history* is unimportant. *Family history.* The father is 6 ft. in height, weighing 300 lbs. The mother has a normal endocrine makeup.

Physical examination. The patient weighed 205 lbs. From symphysis to vertex he measured $33\frac{1}{2}$ in. (85 cm.); from symphysis to soles of the feet, $32\frac{1}{2}$ in. (82.5 cm.). The span was $66\frac{1}{2}$ in. (168.5 cm.). There was very marked adiposity, more or less universal, but definitely increased about the pelvis and shoulder girdles and upper

portions of the thighs. The mammæ were overdeveloped. There was a slight amount of hair in the axillæ and over the mons and a lanugal growth on the face. The head was small. The hands were fairly well developed and normal in size. No definite pigmentation was seen. There was very marked genital aplasia, particularly of the penis:

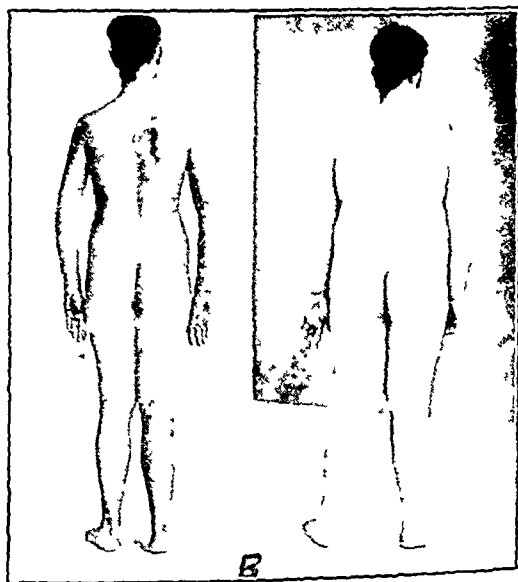
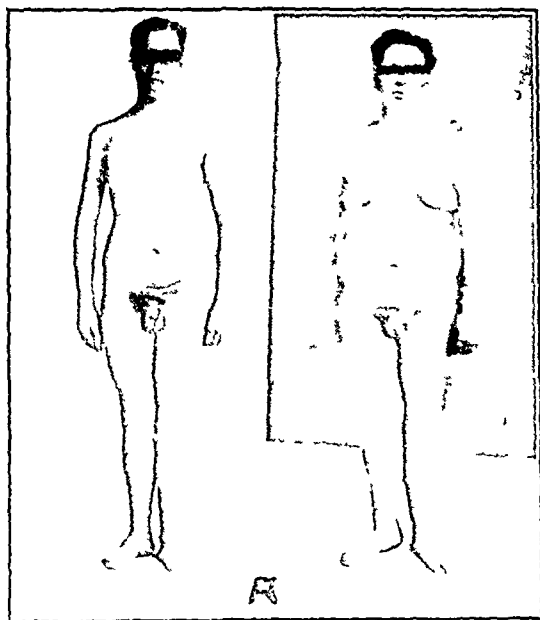


Fig. 3 (A) Case III, age 15. Note the remarkable change following treatment—definite decrease in obesity and striking change in genitalia. Despite definite contour changes, there still is suggestion of feminine type. (B) Posterior view of the same subject.

The measurements were as follows: Bust, 39½ in. (100 cm.); level of navel, 40½ in. (102.75 cm.); level of anterior, superior spine, 43½ in. (110.25 cm.); thigh, upper third, 27 in. (68.5 cm.); middle of leg, 15 in. (38 cm.). Diffuse hyperesthesia was manifest over the entire body. The pulse rate was 80; the blood pressure, 140/80. *Regional.* The frontal incisors were slightly separated. The teeth, generally, showed early decay. The thyroid was not palpable. There was a slight systolic murmur at the apex, disappearing on complete inspiration. A similar murmur, with the same characteristics was observed in the pulmonic area. Large fat folds were seen along the lateral upper aspects and lower portion of the abdomen.

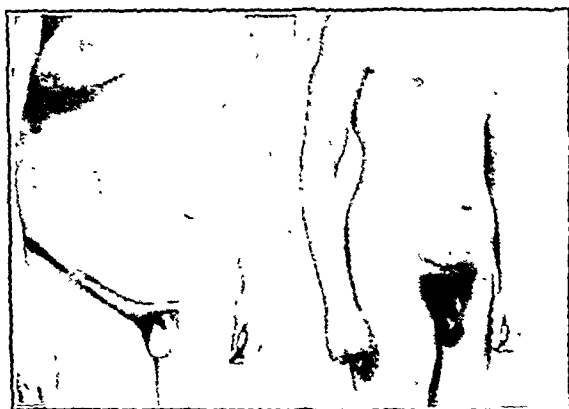


Fig. 4. Close-up of the genitalia of Case III before and after treatment. Note the striking loss of obesity about the breasts, hypogastrum, and mons, although there still is evident a remnant of hypogastric padding. Note also the increased genital development.

The urine was negative. The hemoglobin in the blood tested 95%; leucocytes, 10,500; erythrocytes, 5,420,000. Wassermann examination was negative. *Carbohydrate tolerance.* The blood-sugar, after a fifteen-hour fast, tested 0.054%; the first hour, after 1.59 gm. dextrose per kg. of body weight, 0.132%; the second hour, 0.068%. The basal metabolism was -18%. The *antuitrin* thermic test produced 0.2 degree rise in temperature in fifteen hours.

Radioscopy showed normal carpal, metacarpal and phalangeal bones and no tufting or mushrooming.

The patient passed from observation and was not seen again until two years later. The treatment had consisted of from four to six months' administration of the following: (1) anterior lobe pituitary substance, 2.5 grains, and pituitary substance, entire gland, 10 grains, three times a day, after meals; (2) "Antuitrin" 1 cc. hypodermically, daily; (3) "Pituitrin 0" hypodermically, daily, beginning with a dosage of 5 minims and increasing gradually to tolerance. Notation shows the remarkable loss of weight and comparative changes in measurements which may be noted from the table, complete disappearance of the somnolence, headaches, precordial pain, etc., and gradual development of libido, nocturnal pollutions, erections, and decided genital growth.

Comparative Table of Measurements

	June, 1920	April, 1922
Weight	205 lbs.	149½ lbs.
Height	5 ft. 4 in. (162.5 cm.)	
Symphysis to vertex....	32½ in. (82.5 cm.)	31 in. (78.75 cm.)
Symphysis to soles of feet	31½ in. (80 cm.)	37 in. (93.75 cm.)
(Apparent discrepancy due to convexity associated with former obesity.)		
Span	66½ in. (168.5 cm.)	72 in. (182.5 cm.)
Bust	39½ in. (100 cm.)	35¼ in. (89.25 cm.)
At level of navel.....	40½ in. (102.75 cm.)	29 in. (73.5 cm.)
At level of anterior, superior spine	43½ in. (110.25 cm.)	34 in. (86 cm.)
Thigh, upper third.....	27 in. (68.5 cm.)	21¼ in. (53.75 cm.)
Middle of leg.....	15 in. (38 cm.)	14 in. (35.5 cm.)

As may be noted from the study of the comparative photographs, there has been a remarkable change in general makeup, marked loss of weight, with redistribution of obesity. The padding about the mammary region has disappeared, although still showing slight prominence. The padding in the epigastrium and over the mons has practically disappeared. The hips, formerly convex, now show concavity, with slight fullness about the upper thighs. The obesity, although less, is still suggestive of the former makeup. Although the makeup is more masculine, there is still a suggestion of the habitus femininus, especially in the distribution of the pubic hair. Remarkable growth in the genitalia has occurred, the present size of the penis being 7.5 cm., and the length of the testes, 5 cm.

The above case exhibits a classical preadolescent bilobar insufficiency, the anterior lobe deficiency being represented by the infantile genitalia, the posterior lobe deficiency by the adiposity. There has been a decided response following the institution of treatment, although care must be exercised not to fall into the danger of the *post hoc* argument, because of the well-known fact that similar spontaneous changes do occur without the exhibition of medication.

CASE IV. T. K., GEN. NO. 2951, MALE, AGED 12

Chief complaints. The subject complained of obesity and genital hypoplasia. There was dyspnea after moderate exertion. A tendency to hypersensitiveness, with moderate emotionalism was noted. These symptoms had been manifest for six years (dating back to the removal of the tonsils and adenoids at that time). There had been gradual gain in weight, including 30 lbs. during the last year, but no collateral history of vertigo, syncope, edema, scotomata, headache, polyuria, polydipsia, etc. The father does not believe that there has been proper genital development.

The *past history* is unimportant, except for the removal of the tonsils and adenoids, to which the symptomatology dates. It may be stated parenthetically that it has not been uncommon to find an endocrine syndrome apparently dating to this procedure. The *personal history* is negative. *Family history.* There is marked obesity on the paternal side, the father's brothers weighing from 265 to 400 lbs.; one uncle has diabetes.

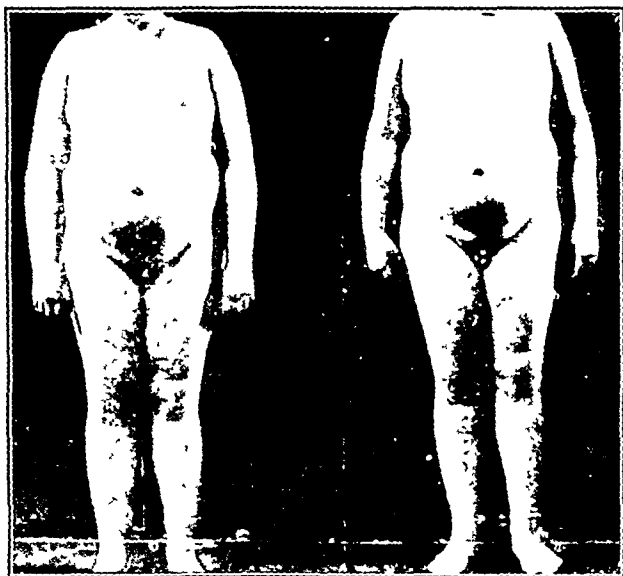


Fig 5 Case IV, age 12 Note the redistribution of fat and the definitely increased genital development. (For comparative measurements, see text.)

Physical examination. The patient was 199 lbs. in weight and 5 ft. 6 in. (167.5 cm.) in height. Measurement from the symphysis to the soles of the feet was 35 in. (88.75 cm.); from symphysis to vertex, 31 in. (78.5 cm.). The span was 70 in. (177.5 cm.). There was definite obesity of girdle type, padding on the lateral aspects of the hips, extending down to the junctures of the middle and lower portions of the thighs, and some fullness about the hypogastrium and mons. The fingers were long and tapering, with some padding on the dorsa of the fingers and hands. Slight supraclavicular padding was seen. The skin was somewhat dry, without infiltration. The head was normal except for padding anterior to the ears and about the angles of the jaw. The ears were normal. The eyes were normal except for thinning of the brows at the outer halves. There was slight high saddling of the nose. The mouth and teeth were normal. The neck was short and obese. The chest, heart, abdomen, genitalia, rectum and reflexes were normal.

The urine was negative. The blood, including the Wassermann test, was normal. Functional kidney test showed 35% phenolsulphonephthalein in two hours. Sugar tolerance test: The blood sugar, after a fifteen-hour fast, tested 0.104%; one hour later, following ingestion of dextrose (1.59 gm. per kg. of body weight), 0.185%; two hours after dextrose, 0.150%. The basal metabolic rate was -20%.

Pituitrin test. One cc. of "Pituitrin 0" injected subcutaneously showed a prompt depressor effect, occurring within ten minutes and persisting for one hour, showing a drop in the systolic pressure of 20 mm., with no appreciable change in the diastolic reading except a brief initial rise. The pulse was definitely decreased—from 110 to 90.

Adrenalin (Goetsch) test: One-fourth cc. (1:1000 solution) injected subcutaneously showed a brief and transient rise, occurring in both systolic and diastolic pressures at the end of thirty minutes, returning to normal in forty-five minutes, with no appreciable change in the pulse.

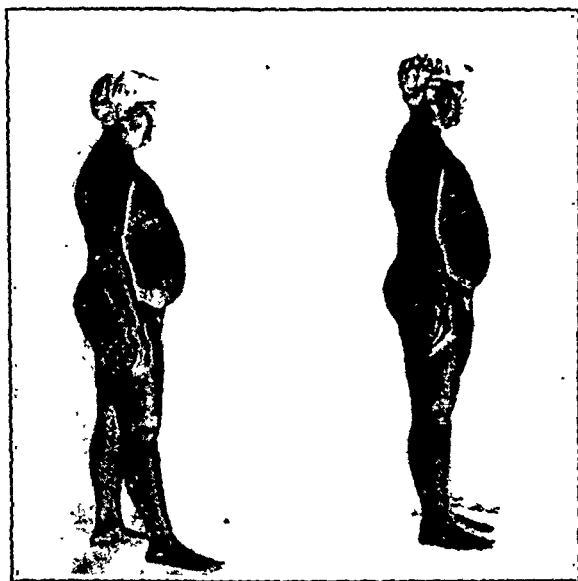


Fig. 6. Lateral view of subject, Case IV, showing definite decrease in adiposity.

Radiogram of the skull. The sella turcica in anteroposterior diameter measured 10. mm.; depth, 8 mm. Anterior and posterior clinoid processes were well visualized; there was no erosion nor excavation. *Radiogram of the hand* showed that all carpal centers were present, that there was no delay in ossification and that ungual phalanges were tapering.

Diagnosis. The case was diagnosed as hypopituitarism, bilobar, preadolescent, associated with secondary hypothyroidism. The following treatment was instituted: (1) pituitary substance, entire gland, $\frac{1}{2}$ gr. after meals; (2) "Pituitrin 0," 15 minims hypodermically, weekly. Two months following the institution of this treatment, the following notation was made: "Patient completely changed. Formerly a marked disinclination for physical work, content to sit and read by the hour; whereas now patient takes a very active interest in baseball and other sports of boyhood and has disinclination to sedentary pur-

suits. Is very much more alert, cerebration increased, with better progress in school. No decided loss in weight, but marked redistribution, decided diminution in obesity about face and neck, loss of 7 in. ($17\frac{3}{4}$ cm.) about waist and 3 in. ($7\frac{1}{2}$ cm.) about hips. Most striking change has been definite increase in size of the genitalia, which can be appreciated from comparative photographs." Observations made four months later showed still more striking changes. The redistribution of adiposity was more definite, particularly about the hips, the lateral surfaces of which were assuming a more masculine character. The abdominal pads were decreased in size, likewise those over the mons. The genitals showed pronounced development, particularly the testes. The penis was somewhat increased in length, and the patient had definite erections. The scrotum was developing, separating from the perineum. The pubic and axillary hair had appeared since the last observation. There was desire for male companionship and boyhood sports, and alertness and capacity for leadership were strikingly increased.

CASE V. MR. G. K., GEN. NO. 1637, MALE, AGED 39*

Chief complaints. Extreme somnolence was manifest in the daytime and insomnia at night. There was enormous obesity, weight being 346 lbs. Marked thickness and harshness of the skin was noted, with padding about the neck, hands and feet. There was disturbance of speech, due to thickness of the tongue, and dribbling of saliva. Dyspnea was marked. There was diminution of visual acuity, loss of libido and impotency. *Duration.* These symptoms had lasted for eight months. The history was elicited with great difficulty because of inability to keep the patient awake. He fell asleep while answering questions, and, when aroused, had no memory of the former interrogation. He was insensitive to ordinary stimuli, requiring hard shaking to arouse. The obesity dated to the age of fourteen, at which time he weighed 120 lbs. At the age of twenty-three he weighed 170 lbs.; at twenty-seven, 220 lbs.; and at thirty, 250 lbs. Eight months ago, weight was 291 lbs.; three months ago, 310 lbs.; at the time of examination, 346 lbs. Somnolence began eight months ago, gradually increasing in intensity, until at this time the patient was wont to go to sleep while walking, eating, or attempting conversation. The voice had become inarticulate; his speech was slurring and mumbling. The skin had become harsh, coarse, thick, and dry, comparable to leather. He perspired freely about the face and upper chest (the remainder of the body was dry). Complete loss of libido had occurred in the past three months, and visual disturbance in the past six months.

Past history. The patient had measles, mumps, chicken pox and diphtheria in childhood, and small pox, pneumonia, and pleurisy in adult life. *Personal and family history* are unimportant.

Physical examination. The subject was 6 ft. (182.75 cm.) in height, and 346 lbs. in weight. There was marked obesity, universal,

*Reported in full in Tice's Practice of Medicine. W. F. Prior Company, Inc., Hagerstown, Md., 1922, 8, 587. (Pituitary Hibernation or Somnolence Wm. Engelbach & J. L. Tierney.)

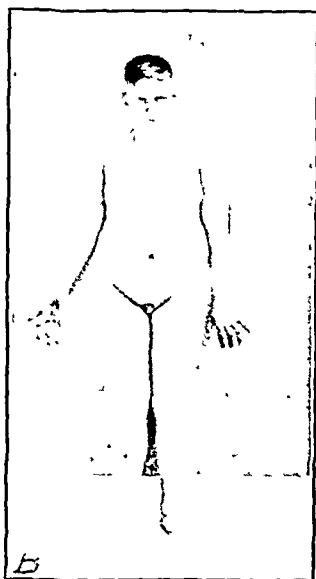
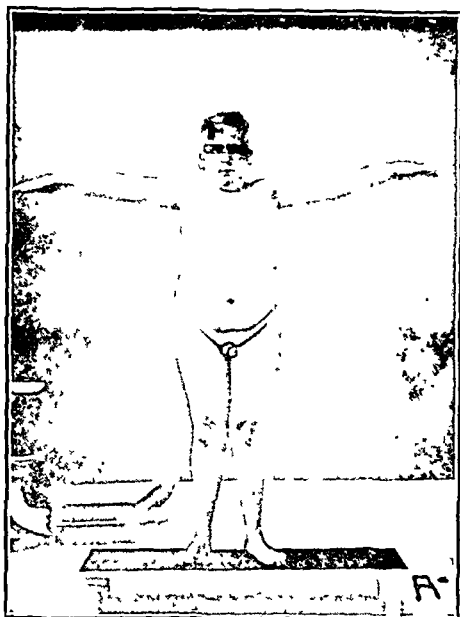


Fig. 8. (A) Case demonstrating hormonal signs of bilobar hypopituitarism. Note the characteristic girdle obesity and genital hypoplasia. (B) Bilobar hypopituitarism, demonstrating the characteristic obesity and genital hypoplasia

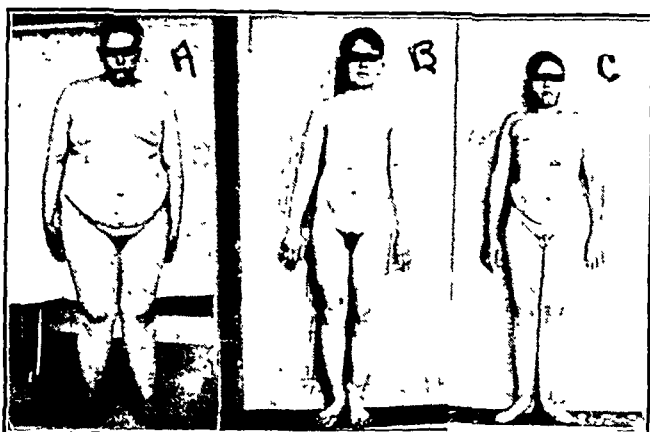


Fig. 9. Varying grades of hypopituitarism, boys of approximately the same age, all showing osseous underdevelopment and genital hypoplasia, representing anterior lobe pituitary deficiency. Case B shows slight obesity suggestive of posterior lobe deficiency. Case C shows this adiposity to a greater degree, as may be noted in the padding about the hypogastrum and mons and the feminine contour of the hips. Case A shows the combined deficiency adiposity plus genital hypoplasia, representing Froehlich's syndrome, or bilobar hypopituitarism (preadolescent).

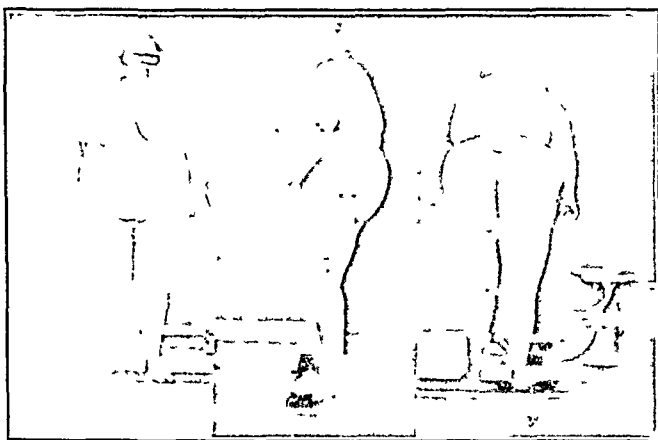


Fig 10 Note the characteristic girdle adiposity with fullness about the hypogastrium mons, and hips extending to the juncture of the lower and middle thirds of the thigh. Note the gracile character of the legs and arms indicating the absence of a thyroid element.

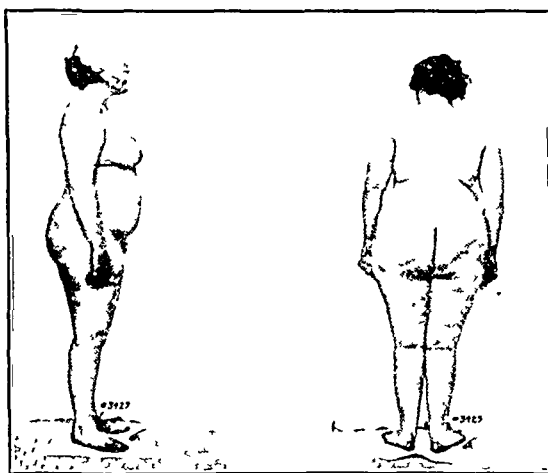


Fig 11 Hypopituitarism, with the characteristic girdle obesity. Note the sharp delimitation at the lower portion of the thigh.



Fig 12 Demonstrating the characteristic pituitary obesity

SUMMARY OF CASES

The series studied consists of 1995 cases displaying endocrine abnormality, as manifest by their hormonal signs. Of this number 711 showed pituitary disturbance (285 purely pituitary, and 426 pluriglandular with pituitary involvement). The cases demonstrated and reported in detail above are representative types, showing more or less objective response to treatment, if we do not fall into "*post hoc ergo propter hoc*" error. There have been many failures, but there likewise have been very many apparent responses with careful clinical control. When, in a large series of cases, these responses in given types to given treatment occur often and with great regularity, we begin to get away from the coincidental and the *post hoc* idea, and approach conviction and a reasonable certainty that more than a casual relationship exists. Careful clinical observations are facts, as truly as biochemical, physiological, or pathological facts, though we admittedly often err in our interpretation. Inde-

pendent of the purely objective, there have been numerous subjective and apparently specific clinical responses to endocrine therapy that do not lend themselves to convincing visualization, especially for hypercritical minds. There have occurred relief of headaches, visual disturbances, psychic states, tachycardia, gastro-intestinal upset, constipation, dysmenorrhea, menstrual changes, decreased cerebration, incapacity, etc., that cannot be measured in millimeters or weighed in grams, but still they stand as clinical facts, so often recurring that they carry a modicum of conviction. Rest, change of climate, forced feeding, static sprays, hypnotism, Christian Science, blue lights, tamponades, I. Q. and S. or Elixir Taraxacum, and other forms of psychic treatment might accomplish the same results; but in most of the cases we speak of, several, and in some, all of these modes of treatment, had been tried without result.

We do not advocate endocrine therapy in so-called primary anemia, carcinoma, gastric ulcer, tonsillitis, aphthous stomatitis, or erysipelas, nor do we advise suprarenalectomy for epilepsy; but when, in a series of cases showing what we believe to be demonstrable harmonic evidence of endocrine disturbance, with subjective symptoms not due to other demonstrable causes, in which we repeatedly find response to indicated endocrine therapy, we feel that we must assume a casual relationship.

In the present state of our knowledge, it is no time for futile battle. Let us remember that vitriolic verbiage is no argument. Let us all, chemist, pathologist, physiologist, and clinician, realize that we are co-operative observers, all honestly and painstakingly marshalling facts that we may in harmony correlate, and thus further our knowledge in a perplexing, though interesting, field.

CONCLUSIONS

- (1) There is remarkable discrepancy and lack of co-ordination in our available evidence concerning the function of the pituitary gland, considered either in its entirety or from the standpoint of its component lobes.
- (2) There is little definite knowledge concerning the chemistry of the gland.
- (3) The anterior lobe conforms to the requisites of a secretory gland, whereas the pars nervosa does not, being purely

nervous tissue; unless we take into consideration the pars intermedia as being the essentially secreting portion of the posterior lobe, realizing, too, that the pars intermedia is developmentally similar to the anterior lobe.

(4) We have no assurance that what we term *posterior lobe* extract, with apparently more demonstrable physiological effect, represents the true internal secretion of the gland, and can have no such assurance until the substance or active principle is demonstrated in the efferent blood or lymph of the gland, and no adequate available supply until this substance is synthesized and accurately standardized.

(5) Experimentation has taken insufficient account of the essential biological differences between the human being and experimental animals, a typical discrepancy being the consistent pressor effect as the result of pituitary extract in animals on first injection, and the frequent opposite effect in the human being, at least in our experience.

(6) Concerning the efficacy of the desiccated preparations of the gland, we have contradictory evidence. The value of pluriglandular therapy on the basis of a cell selectivity is being overpopularized; and, while one must realize the frequency of pluriglandular combinations and the almost absurd number of possible pathological combinations, sufficient attention must be paid to uniglandular therapy or the *rational* combination of glands based upon the presenting hormonal signs, and to the fact that pluriglandular imbalance may occur as the result of a lesion in one gland and may be restored by correcting the function of that particular gland.

(7) Therapy should be based upon the presenting hormonal signs, and, if these signs warrant, should be uniglandular, or even unilobar; and if other glands are apparently involved, an associated therapy should be instituted, but one based upon the presenting symptomatology.

(8) The literature has been flooded with reports concerning the response of isolated symptoms to pituitary therapy, without sufficient collateral detail concerning the type (osseous and genital makeup, obesity, dermal, chemical, or metabolic changes) or proper attempt at conformation to type.

(9) Upon what was deemed a judicious selection of evidence concerning the functions of the component lobes of the pituitary and their representative harmonic signs, a purely tentative classification was formulated, as it was felt that study along more specific lines would further our knowledge and enable us more quickly to negate or verify conflicting contentions concerning this gland.

(10) To secure the best results, therapy should be instituted early in the course of the disease, which implies early diagnosis. After pluriglandular involvement has occurred, a state usually resulting within a year, responses to therapy are less certain.

(11) The observation of a large number of cases to date, in which therapy was based upon the presenting symptomatology, has shown numerous responses, both subjective and objective—responses that have occurred so frequently that we have become convinced of more than a casual relationship and consider ourselves warranted in persisting in clinical studies along these lines.

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THE FUNCTION OF THE LOBES OF THE HYPOPHYSIS AS INDICATED BY REPLACEMENT THERAPY WITH DIFFERENT PORTIONS OF THE OX GLAND*

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The proper administration of an endocrine principle should correct an abnormality due to the deficiency of this principle.† In the tadpole four such rather sharply defined abnormalities result from early hypophysectomy,§ namely, (1) a slowed growth rate; (2) an underdevelopment of the interrenal bodies, parathyroids and thyroid with a consequent failure of the larva to metamorphose; (3) an abnormal condition of the pigment bearing cells resulting in albinism; and (4) a large and persistent fat organ which we are inclined to believe indicates a disturbance in metabolism. We should, by the proper administration of the hypophysis be able to correct these disturbances or, indeed, to go further and by the administration of the separate lobes determine which lobe when administered will remedy a particular abnormality and in this way analyze the functional nature of each of the lobes of this composite gland. The pituitary of the mammal (beef) lends itself readily to such an analysis.

Our experiments point to the conclusion that several principles, namely, that controlling (1) general body growth and the development of certain of the endocrine glands, (2) the behavior of the pigmentary system, and (3) the capacity of the fat organ to respond to nutritional conditions, are present in the hypophysis of the beef. Certain of these principles are found only in a single lobe; other principles are common to more than one lobe.

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†We would hardly expect, however, to correct a condition of skeletal overgrowth; thus it would obviously be impossible to shorten the abnormally long bones of the extremities of the eunuch by the exhibition of testicular substance.

§By the term "pituitaryless" or "hypophysectomized" we refer to the loss of only the epithelial or buccal derivatives of this gland, not to the neural derivative, the posterior lobe. However, since in the specimens which have suffered the early loss of the buccal anlage of this gland the neural lobe is undersized, there is probably a deficiency in the secretion of this lobe also. Due to the metallic white appearance induced by hypophysectomy the animals are spoken of as "albinos."

hyperplasia result. The scanty adrenal cortex of the albino becomes normal with injections of anterior lobe substance.

The *feeding* of anterior lobe does not elicit any response from the atypical glands of the albino (Smith, 1), actual injection of the substance being necessary in order to effect their repair. These effects on the thyroid from the injections of bovine anterior hypophyseal substance are in accord with transplantation experiments in amphibia [Allen (6), Swingle (8)].

The Pigmentary Response. Albinos injected with the anterior lobe darken perceptibly within a few hours after such injections; after several injections at intervals of two days each they become as dark as normal specimens.† In addition to this darkening in color tone, those injected with the anterior lobe exhibit a definite and unmistakable reddish tone which progressively becomes more pronounced during the metamorphic stages.

The microscopic examinations of the living specimens and of cutaneous whole mounts reveal the fact that both the melanophores and the xantholeucophores have lost the characteristics which they invariably display in the typical pituitary albino.

The epidermal melanophores have increased in number to approximately that occurring in the normal specimen, have lost to a considerable degree their persistent contraction, and have become approximately normal in their melanin content. The free epidermal pigment (melanin) which is characteristically greatly reduced in the albino is as abundant in these injected specimens as in the normal controls. It has been previously pointed out that in the typical pituitary albino the xantholeucophores, which form a double layer over most of the body, display a pronounced and persistent expansion and that to this expansion is referable the metallic white color so characteristic of the pituitary albino (Smith, 12). In the anterior lobe-injected pituitaryless tadpole these cells appear to be greatly contracted, a condition which apparently obtains in the normal, and are usually so described, a description with which we have heretofore agreed. Such a description, however, as a study of our injected albinos shows, has been based upon observations made upon the guanine content of these cells, the xanthine constituent being normally so slight in amount as to escape clear observation. In our hypophysectomized tadpole, injections of anterior lobe substance have caused a great increase in this latter constituent to which is due the above-mentioned reddish tone which these specimens display so that observations can now be made upon both the guanine and xanthine constituent of these cells with great reliability. Such observations show that while the refractile substance, guanine, is always centrally clumped, the lipochrome, xanthine, can be seen extending well out into the processes of spider-like cells, intermediate in shape, between

†This darkening in color from anterior lobe injections is not peculiar to the hypophysectomized tadpole. The depth of color is increased in the normal and thyroidless tadpole and a profound darkening results from the injection of this substance in the Colorado axolotl, these animals becoming jet black.

the corial and epidermal melanophores. With this definitely determined, the question immediately confronted us as to whether this condition is peculiar to the injected pituitaryless specimen or prevails also in the normal tadpole. We found this condition to obtain in the normal, where, however, the xanthine content is, of course, slighter in amount. The xanthine thus may form an extensive sheet as in the typical albino or be clumped in a dotlike mass as in the injected pituitaryless or normal tadpole, without the xanthine undergoing the same changes. The different behavior on the part of these two pigments would appear to lend considerable support to the contentions of Schmidt (13, 14) that these two substances are borne by separate cells, paired and intimately associated, not by a common cell as Gaupp, Biedermann, Fuchs and others believe, and which caused them to use the term "xantholeucophore." For it seems improbable that two types of pigment within a cell would move independently of each other. The statement of Hooker (15) would appear to be as pertinent in this connection as in the discussion of cytoplasmic movement in the melanophore in which he pointed out that the assumption of an independent movement of two types of cytoplasm within a single cell is "unique in the animal kingdom" and states "the control by which such a process, alternately causing expansion and contraction of the one type of protoplasm within the other might go on indefinitely, is by no means clear."

The Behavior of the Fat Organ. The fat organ which attains an unusual size in the pituitaryless tadpole [see Fig. 60, Smith (1)], and persists even in starvation in contrast to the disappearance of this body in the normal tadpole under similar conditions is always reduced to normal dimensions in the hypophysectomized specimens which have been injected with anterior lobe substance. We have been inclined to believe that the enlarged condition of this "organ" is an indication of a disturbed metabolism and corresponds to the adiposity induced occasionally by operations on, or in the neighborhood of, the hypophysis of the mammal. If such a comparison be correct, then the injection of this lobe of the pituitary should reduce in the mammal the adiposity which may be instituted, experimentally, by operative procedures on the hypophysis.

II. THE PARS NERVOSA

Two of the abnormalities exhibited by the hypophysectomized tadpole, namely, the adiposity and albinism, are corrected by the injection of neural lobe substance, the latter being but imperfectly so, however. It must be emphasized here that we have injected pure pars nervosa substance uncontaminated by the intermediate lobe. The fat organ is reduced in size by the injection of pars nervosa in contrast to the large size normally obtaining in the pituitary albino.

What has been already described in regard to changes in

pigmentation with anterior lobe injection may be stated in regard to the responses of this system with posterior lobe injection, but with this modification, namely, that the return to a normal pigmentation does not develop so rapidly nor is it so complete as with anterior lobe injections. A greatly prolonged series of injections (3-4 months) may bring about a nearly normal coloration.

There is no effect upon growth, nor does the injection of posterior lobe cause any response in the thyroid or interrenal body of the albinos, the specimens remaining larval.

III. THE PARS INTERMEDIA

As with injections of the other two lobes of the pituitary the size of the fat organ is reduced by injections of the intermediate lobe. The immediate pigmentary response elicited by intermediate lobe injections is usually more pronounced than that given by either the neural or anterior lobe; the ultimate effect does not appear to transcend that given by the latter division of the gland. No unquestionable growth response is given, though the specimens usually become somewhat longer and relatively more slender than their untreated pituitaryless controls. This characteristic is distinctive for this treatment. No change is effected in the thyroid nor interrenal substance, legs do not develop and no other signs of metamorphosis are apparent.

IV. COLLOID

Injections of colloid substance produce a darkening of the albino, though a normal depth of pigmentation is not attained even when injections are carried out over a long period. No growth nor endocrine responses result and the specimens show no signs of metamorphosis. Our findings support the conclusion of Fenger (16) that the colloid of the vestigial lumen is a physiologically inert substance.

The stability of these principles as shown by various treatments. In our attempts to isolate the various principles of the anterior lobe of the beef we have found that the only principle which appears to retain its activity under all of the treatments, some of them most severe, to which we have subjected the anterior lobe substance is the principle evoking a reaction from the

pigmentary system.* A pronounced pigmentary effect was still secured after the anterior lobe had been boiled in distilled water, or in 0.3 per cent hydrochloric acid for several hours, a treatment which Hogben and Winton (17) found diminished the activity of the "melanophore stimulant" of the posterior lobe; the effectiveness persisted also after drying, taking no precaution to guard against oxidation. No endocrine nor growth responses were given by the anterior lobe after these treatments.

Treatment with alcohol, on the other hand, does not appear to destroy the endocrine principle. After extraction for 48 hours in absolute alcohol the supernatant fluid gave no effect upon the thyroid; however, a definite effect was given by injection of the precipitate. After extraction of the anterior lobe in 8 per cent alcohol for 24 hours the centrifuged supernatant fluid which had been freed from much of the proteins by this extraction gave a pronounced endocrine with a slight growth response, the specimens metamorphosing. The fate of the growth principal has not been ascertained in the alcohol residues, since the specimens absorbed with difficulty the particulate matter and the injections were terminated before the experiment had extended over a long enough period to determine definitely whether this principle were present or had been destroyed.

Both precipitate and supernatant fluid darkened the specimens. A pigmentary response has always been elicited by any hypophyseal substance which we have prepared from the anterior lobe and from both neural and intermediate lobes.

DISCUSSIONS AND CONCLUSIONS

The growth retardation which has been shown to result from hypophysectomy in the tadpole, appears to be definitely due to a deficiency of the glandular lobe of the pituitary. Grafts of the amphibian anterior lobe accelerate growth in the tadpole; injections of the bovine anterior hypophysis, as here shown, cause an overgrowth in either the hypophysectomized, normal or thyroidless tadpole. The specific growth stimulus which is thus given by this part of the hypophysis, the posterior lobe giving no acceleration and the intermediate lobe only a questionable one, would appear to demonstrate that the maldevelop-

*We have not tested the stability of this principle in either of the other lobes.

ments of the hypothalamus due to the early removal of the hypophysis (Smith, 1), plays no part in the growth retardation induced by these hypophysectomies and that they are due to a deficiency of anterior lobe secretion. This would appear to make it highly probable that the growth retardation induced by experimental hypophysectomies in the mammal [Crow, Cushing and Homans (18), Aschner (19)] is directly due to a quantitative reduction in the hormone of the anterior lobe and not, as suggested by Bailey (20), to any incidental injuries to the hypothalamus.* This conclusion is strongly supported by the fact that injections of anterior lobe substance induce a "mild degree of gigantism" in the rat (Evans and Long, 9, 10).

Anterior lobe substance exercises a definite control over at least the thyroid and interrenal glands. Extirpation experiments, obviously, in the tadpole would not make it certain which division of the pituitary exerts this influence, since the anlage ablated is destined to form both intermediate and anterior lobes, and prevents the normal development of the neural lobe. Since injections of the bovine anterior lobe repair the underdeveloped glands, the tadpole then metamorphosing (Smith and Smith, 11), while injections of neither of the other two divisions effects such a repair, it is clear that the anterior lobe alone exerts this reparative or constructive influence on these glands.

It would appear to us that this response of the thyroid to anterior lobe injections is an expression of a constructive influence which the glandular lobe of the hypophysis exercises. A lack of this influence (or stimulation) is apparently seen in the failure of the pituitaryless tadpole to grow at a normal rate and to develop a normal endocrine system. This can be corrected or "over-corrected" with a consequent gigantism and thyroid hyperplasia by anterior lobe injections. It appears that the stimulus to lutein cell formation in the rat which Evans and Long (10) have shown is effected by anterior lobe injections, thus indirectly inhibiting oestrus, may be an expression by this gland of a general constructive or stimulative influence upon the glands of internal secretion.

We have seen that the ablation of the buccal hypophysis brings about a profound derangement in the pigmentary system of the tadpole, the specimens becoming albinous. Skin trans-

*Any direct operative injury to the hypothalamus is absolutely precluded by the nature of our hypophysectomies.

plants have shown that this albinism is due to an alteration in the body fluids, probably of an endocrine origin and not to an altered nervous connection (Smith, 21; 1).

Investigators have referred any pigmentary influence which may be exerted by the hypophysis to the pars intermedia [Atwell (22, 23), Smith (1), Allen (6, 7), Swingle (8), Hogben and Winton (17)]. In this paper we have shown that the injection of each of the three lobes of the bovine pituitary and of the colloid alters the state of contraction of these cells and increases the pigment content of some of them.

The profound effect which this principle has on pigment metabolism, and the broad distribution which it enjoys in the bovine pituitary would make it seem highly probable that it must play some significant rôle in the body of the mammal.* It is surprising that pigmentary disturbances in pituitary dystrophies are not more frequently described.

The enlarged fat body of the albino, we have found, is reduced to normal dimensions by the administration of any one of the three lobes of the pituitary, a reduction which we have not been able to effect by inanition or thyroid administration. This specific response of the fat body appears to demonstrate that its enlarged condition in the hypophysectomized tadpole is due to a pituitary deficiency and not to any abnormalities of the hypothalamus, which develop secondarily. It is pertinent here again to mention that any direct operative injury to the infundibular region is absolutely precluded by the nature of our hypophysectomies.

We realize that these findings in regard to the response of the fat body of the pituitaryless tadpole do not justify us in stating that the adiposity induced occasionally from operations on the pituitary region of the mammal is due to a pituitary deficiency. The gap between the two forms is wide and the "adiposity" of the hypophysectomized tadpole may not be analogous

*The fact that this principle alters the state of contraction of the pigment cells would not indicate that it has specifically to do with pigment changes in the mammal. Thus adrenin, which contracts the corial melanophores (Lieben, 24), alters the state of contraction of smooth muscle also, a fact which has led Spaeth (25) to believe that the melanophore is a disguised type of smooth muscle. Hogben and Winton (17) have shown that there are certain similarities in the behavior of the "melanophore stimulant" and of the uterine stimulant of the posterior lobe when treated with HCl, their action differing from the pressor substance of this lobe. The fact, however, that this principle influences the metabolism of epidermal pigments would appear to make it of importance in the mammal.

Type	Hypophysectomized			Hypophysectomized			Hypophysectomized			Hypophysectomized			Hypophysectomized		
Injection	None			Pars intermedia			Pars nervilis			Pars anterior			Colloid		
	Length in mm.	Vol in cc	No of Specs	Length in mm	Vol in cc	No of Specs	Length in mm	Vol in cc	No of Specs	Length in mm	Vol in cc	No of Specs	Length in mm	Vol in cc	No of Specs
Aug 30	Total Leg 37-40 39	None	8	Total Leg 37-38 37	None	8	Total Leg 36-38 37	None	8	Total Leg 35-41 38	None	8	Total Leg 35-37 36	None	10
Sept 23	36-45 39	None	7	41-44 43	None	8	35-40 39	None	8	41-47 41	None	8	33-39 36	None	9
Oct 20	39-49 43	None	5	48-52 50	None	8	42-52 40	None	8	52-60 53	None	8	36-41 39	None	4
Nov 3	43-45 42	None	3	50-53 51	None	5	42-47 46	None	3	58-67 63	None	7	39-41 40	None	2
Nov. 17	Discontinued			48-49 49	None	4	Discontinued			53-67 63	None	7	Died		

*The specimens which developed legs over 3 mm. in length showed, when sectioned later, small thyroid remnants. These specimens are not included in the remainder of the column.

to the adiposity in the adiposo-genital syndrome of the mammal. Yet the probability of an identical causative factor in the two animal forms should prevent us from too hastily casting aside the earlier concept that the adiposity in this syndrome was due to a pituitary deficiency and substituting in its place the idea that all responsibility for this condition can be laid at the door of the hypothalamus, as some investigators have been inclined to do. Since the principle which will diminish the size of the fat body of the pituitaryless tadpole is present in each of the three lobes of the hypophysis, it is not surprising that adiposity does not usually develop in the mammal in partial anterior lobe removals or in posterior lobe ablations.

SUMMARY

The intraperitoneal injection of different portions of the bovine hypophysis in the hypophysectomized tadpole gives the following results:

1. Pars anterior brings to normality the four deficiencies resulting from hypophysectomy in that it accelerates the growth rate; induces a normal depth of pigmentation; repairs the atrophic thyroid and interrenal bodies, the specimens metamorphosing; and reduces to normal dimensions the fat organ. The normal and thyroidless tadpoles when injected with anterior hypophysis show an acceleration in their growth rate, attaining an unusually large size, and display an increased depth of pigmentation.

2. Pars intermedia corrects the pigment upset and reduces the size of the fat organ.

3. Pars neuralis elicits a moderate pigmentary response and reduces the size of the fat organ.

4. Colloid induces a slight response in the pigmentary system.

Of the various principles in the bovine anterior hypophysis that evoking a response in the pigmentary system appears to be stable, withstanding drying, severe heat, and certain chemical treatments; while those principles accelerating growth and reaction with the endocrine system are more labile, remaining active, however, after treatment with alcohol.

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Book Reviews

EIN EXPERIMENTEEL KRITISCH ONDERZOEK OVER DE OEDEEM-THEORIE VAN EPPINGER. S. van Creveld, Amsterdam, 1922. 128 p.

In 1917 Eppinger published his book, "Zur Pathologie und Therapie des menschlichen Oedems." In it he states, among many other things, his theory that diuresis does not depend upon the kidney alone. In the regulation of water and salt metabolism the complex of the intercellular spaces in the tissues has a function just as important or even more important than the kidney. The most effective drugs that act, not on the kidneys, are the thyroid preparations; these are often very effective in seemingly incurable cases of edema. Thyroid medication, Eppinger believed, acts by breaking down the proteins of the edema fluid. Eppinger's statements have been generally accepted. Van Creveld, however, does not agree with him. On the basis of numerous experiments he concludes that the hormone of the thyroid acts directly upon the kidney. It also increases protein metabolism and the resulting metabolites cause an increase of diuresis. Those who have read Eppinger's book should read this critique by van Creveld. Unfortunately it is written in Dutch, thus preventing most investigators from reading it.—J. K.

IL MORBO DI RECKLINGHAUSEN. N. Samaja, Milano, 1919. Società editrice libraria. 85 p.

Recklinghausen's disease is believed by some to be due to endocrine disorders. The adrenals, especially, are often reported to be involved. Various cases have been described which have been markedly improved by organotherapy, although each investigator seems to have used a different preparation. Samaja's book gives an excellent review of the known data on this subject. Some splendid illustrations and an excellent bibliography increase the value of the book.—J. K.

CONTRIBUCION AL ESTUDIO DE LOS TUMORES DE LA HIPOFISIS. Wehrhahn R. Alejandro. Santiago de Chile. Imp., Lit. y Enc. "La Ilustracion," Calle Moneda, 873. 1922. 175 p. with illustrations.

Reviewed in Am. J. Roentgenol., 9, 834, by James T. Case, who pronounces it a splendid work on the clinical diagnosis and treatment of tumors of the hypophysis.—R. G. II.

THE THYROID GLAND. George W. Crile, M.D., and Associate at the Cleveland Clinic, Ohio. Philadelphia, 1922. W. B. Saunders Company. 228 p.; 106 illustrations.

Reviewed in Am. J. M. Sc. (Phila.), 1922, 164, 750.

DIE OEDEMKRANKHEIT. Prof. Dr. A. Schittenhelm & Prof. Dr. H. Slecht. Berlin, 1919. Julius Springer. 103 p.

The studies reported in this book were completed but publication was forbidden by the military censor.

The edema problem has been of special endocrine interest since Eppinger's investigations concerning the rôle of the thyroid in the pathogenesis of that disorder. Schittenhelm and Slecht have carefully studied the metabolism and the influence of *thyroidin*, *adrenalin* and *hypophysis* on water and salt metabolism in cases of edema. Excretion of water and salt, when not given in large quantities, seems normal. However, *thyroidin* markedly hastens the excretion of NaCl and water, although in health it has practically no influence. The influence of other drugs, such as *adrenalin* and *hypophysis*, is shown in many tables and curves. The book is easy and pleasant to read, but nearly impossible to abstract. The reviewer recommends it very highly to all who are interested in edema. It is greatly superior to much of the endocrine literature.—J. K.

INTERNAL SECRETIONS AND THE DUCTLESS GLANDS. Swale Vincent. Second Edition. London, 1922, E. Arnold & Co., N. Y. Longmans, Green & Co. 422 p. 8°.

Many endocrinologists are already familiar with Professor Vincent's book through the widespread use of the first edition of it.

The monograph is written from a standpoint indicated in the introductory chapter: "It must be confessed," the author says, "that we do not know the functions of any one of the ductless glands in the same definite way in which we know the functions of, for example, the lungs or the pancreas. Owing to the lack of boundaries and the absence of precise exploration in many regions, the territory of internal secretion has been invaded by some irresponsible exploiters. The time has arrived for us to take our bearings and ascertain our precise position with regard to the subject. In doing this, every effort will be made to avoid dogmatism, even at the risk of losing, or hesitating

to accept, some tempting and plausible theories." The chapter on methods concludes: "It seems to the present writer that one of the methods which will yield the most valuable results in the near future is the oldest of all—namely, careful study of clinical conditions and a patient investigation of pathological anatomical findings. Now that the microscopical structure and the comparative anatomy has been worked out with some completeness, and the results of extirpation experiments and the action of organ extracts fairly well known, pathologists may return to the problems with a better foundation of knowledge and fresh hopes for future discovery."

While many worth-while contributions in the enormous mass of the endocrine literature have necessarily been omitted, the author has on the whole chosen his material judiciously. In the opinion of the reviewer, the book is the best of its scope in the English language for the student wanting a good general command of the subject of endocrinology.—R. G. H.

DIE KONSTITUTIONELLE DISPOSITION ZU INNEREN KRANKHEITEN.

Dr. J. Bauer. Second Edition. Berlin, 1921, J. Springer. 650 p.

Much space is devoted to endocrine factors and their importance in determining constitutional make-up. There is much to be learned from every page, and no one who reads this splendid book will regret the time devoted to it.—J. K.

MODERN METHODS IN THE DIAGNOSIS AND TREATMENT OF GLYCOSURIA AND DIABETES. Hugh Maclean, M.D., D. Sc., M.R.C.P. Constable & Co. 159 p., 13 charts, 9 figures. Price, 12s.

Reviewed in Irish J. M. Sc. (Dublin), 1922, 5s., 484.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. Hrsg. v. Emil Abderhalden. Abt. V., Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus, Tl. 3 A, H. 3, Lief. 69. Curt Herbst, Günther Hertwig, Benno Romeis & Hermann Braus. Urban u. Schwarzenberg, 1922, Berl. u. Wien. pp. 441-538.

Reviewed in Ber. ü. d. ges. Physiol., 15, 357.

Abstract Department

Sensitization of the Trendelenburg frog preparation for the determination of ADRENALIN (Sensibilisierung des Trendelenburgschen Frosch-präparates zur Adrenalinmessung). Alday-Redonnet (T.), Biochem. Ztschr. (Berl.), 1920, 110, 306-318.

The addition of 0.1% more KCl to the perfusing Ringer's solution markedly sensitizes the Trendelenburg preparation. An alkaline reaction of the perfusion fluid has the same effect. The optimum lies around $\text{pH}=10.5$ in phosphate buffer solution. The spontaneous sensitization which occurs in the usual preparation is due to a diminished acidity.—F. S. H.

ADRENAL insufficiency (Breves consideraciones sobre insuficiencia surrenal). Alvarez (W.), Semana méd. (Buenos Aires), 1922, 29, 869-872 (October 26).

The author diagnosed adrenal insufficiency in a case of acute peritonitis, one of "typomalaria" and one of chronic malaria. In the first two cases adrenalin ameliorated the symptoms.—B. A. H.

Intracardial ADRENIN injection for acute heart failure (Intrakardiale Adrenalininjektion bei akuter Herzlähmung). Baumann (E.), Schweiz. med. Wchschr. (Basel), 1923, 53, 198-200 (February 22).

Report of 2 cases of heart failure of young children successfully treated. The recommended dosage is 0.5 cc. "adrenalin" for children under six months of age and proportionately larger doses up to 1.25 cc. for adults.—R. G. H.

The cholesterol and lipid phosphorus contents of the blood of rabbits before and after SUPRARENALECTOMY. Baumann (E. J.) & Holly (O. M.), J. Biol. Chem. (Baltimore), 1923, 55, 457-475.

Rabbits were suprarenalectomized, usually in two stages, and the basal metabolism, blood lipoids and other determinations made frequently. The results show that there is no evidence for the hypothesis that the adrenals are the seat of cholesterol formation. Nor is there any reason to suppose that the glands act as a storehouse for cholesterol.—F. S. H.

Sudden death in a soldier presenting marked fibrosis of the ADRENALS (Morte subite chez un militaire présentant des lésions de surrenalite sclereuse). Bazin, J. de méd. et de chir. prat. (Paris), 1918, 89, 735-738.

This is a report of the case of a soldier aged 35 years, who after an attack of "grippe" complained of fatigue, followed by nausea and vomiting. There was no pigmentation of the skin. "Ligne blanche" was absent. Death occurred suddenly, after a short period of dyspnoea and cyanosis. At postmortem examination marked fibrosis of both adrenals was found. Bazin thinks that adrenals which are the site of such a chronic inflammatory process may be a factor in sudden deaths after acute infections like "grippe."—J. P. S.

A case of intoxication by ADRENALIN (Ein Fall von Adrenalinvergiftung). Bornstein, *Klin. Wchnschr.* (Berl.), 1922, 1, 1484; see also *Deutsche med. Wchnschr.* (Berl.), 1922, 48, 1400.

Ten years ago a doctor intravenously injected into himself 1 mg. of adrenalin. After severe collapse, Bright's disease developed; orthostatic albuminuria remained for some time, but at the time of the report the only symptom was renal glycosuria.—J. K.

Treatment of epileptic spasms by ablation of an ADRENAL (Zur Behandlung der epileptischen Krämpfen mit Exstirpation einer Nebenniere nach Brüning). Borszéky (K.), *Zentralbl. f. Chir.* (Leipz.), 1922, 49, 1053-1057.

The author removed an adrenal in each of 9 cases of epilepsy. The operation seems to have no evil consequences. Although not one case was cured after operation, there was usually temporary improvement. The author recommends the ablation of the right adrenal, since it is often heavier than the left.—J. K.

Incoercible vomiting of pregnancy with acidosis. ADRENALIN carbohydrate treatment. Therapeutic abortion. Psychic troubles. Cure (Vomissements incoercibles de la grossesse avec acidose. Echec du traitement hydrocarboné-adréraline. Avortement thérapeutique. Troubles psychiques. Guérison). Cathala & Biancani, *Gynéc.* (Par.), 1922, 24, 615-616.

Syphilis of the ADRENALS. Deaderick (W. H.), *Am. J. Syph.* (St. Louis), 1923, 7, 72-82.

An excellent review of the literature and report of a case. A woman of 40 with positive Wassermann reaction developed, among other changes, weakness, slight hypotension, anemia and very marked pigmentation. A diagnosis of probable Addison's disease was made. After 3 weeks' treatment with mercury and adrenal gland substance the systemic symptoms, but not the pigmentary condition, were improved. A month after discharge the patient reported that the discoloration was fading.—R. G. H.

Effect of muscular activity on perfused ADRENIN. Hoskins (R. G.) & Durrant (E. P.), *Am. J. Physiol.* (Balt.), 1923, 63, 404-405 (Proc.).

The systemic reactions to adrenin perfused through the limb of a dog or cat are not decreased after severely fatiguing the limb. It is suggested that adrenin is probably a respiratory catalyst.

—T. C. B.

ADRENAL syphilis (*Syphilis das glandulas suprarrenes*). Figueredo (C. B. de), *Comunic. 3a Conferencia de Higiene Microbiologia e Patologia*, Montevideo, 1923.

Description of 90 cases of syphilis, with histologic study of the different organs and especially of the adrenals, the latter showing lesions in 75 cases. The following disorders were seen: lymphatic and plasmatic infiltrations, para- or sub-capsular, rarely in the cortex (63%); thickening of the gland with perivascular infiltration (31%); and circumscribed fibrosis (3.3%). The spirochetes were found in the zones of leucocyte infiltration. The frequent appearance of adrenal lesions in syphilitic subjects (83%) should render this gland of valuable diagnostic assistance at autopsy.—B. A. H.

Colorimetric and pharmacologic evaluation of the ADRENALIN content of the ADRENALS (*Die Kolorimetrische und pharmakologische Auswertung des Adrenalingehalts der Nebennieren*). Frowein (B.), *Biochem. Ztschr. (Berl.)*, 1923, 131, 559-666.

The colorimetric method gives too high results and should be replaced by the blood-pressure method.—F. S. H.

Urine acidity after the injection of ADRENALIN chloride. Hubbard (R. S.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 20, 187-189.

The tests were made on the author. Two tablets were given showing the effects on the blood, breath, and urine after 1 cc. of a 1-1000 solution was injected subcutaneously. There was only a slight change in the acidity of the urine.—J. C. D.

The influence of the injection of ADRENALIN into the subarachnoid cavity on body temperature. Ikeda (S.), *Chugwai Iji-Shimpo*, 1922, No. 1013.

The subarachnoid injection of adrenalin results in a slow and gradual rise of the body temperature.—*Jap. Med. World*, 2, 325.

Calcium content of the serum after ADRENALIN injection. Inouye (T.), *Tokyo Igakkai Zasshi*, 1922, 36, No. 6 (June); *abst., Jap. Med. World (Tokyo)*, 1922, 2, 331.

Although there occur quantitative changes in the calcium contents of the urine after adrenalin injections, there develop no changes in the calcium contents of the blood as they have been estimated at 10, 15 and 30 minutes after the injection.—R. G. H.

The musculature of the venous walls in the human suprarenal and its relation to the action of ADRENALIN. Kashiwagi (M.),

Nisshin Igaku, 1922, 11, No. 10 (June); abst., Jap. Med. World (Tokyo), 1922, 2, 327.

The author points out in the parenchyma of the suprarenal capsules the presence of groups of longitudinal smooth muscle fibers in the venous walls which are connected directly with the perivascular membrane. These are the results of the continuous stimulation by adrenalin and they become more and more prominent as the age advances.—R. G. H.

Anencephalia and the ADRENALS (Anenzephalie und Nebenniere).

Kohn (A.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1666.

Anencephalia and hypoplasia of the adrenals are sometimes found together. The author believes that primary to hypoadrenalism a change is always found in the hypophysis of anencephalic monsters (no infundibulum and no pars nervosa); in the pars anterior the oxyphil cells are rare, and many peculiar large basophil cells are found. The adiposity of anencephalic subjects may be explained also by hypophyseal changes.—J. K.

Blood features after the injection of ADRENALIN, especially on the numerical changes of the blood platelets. Kubo (K.), Nippon-No-Ikai, 1922, 12, No. 21, No. 22; cit. Jap. Med. World (Tokyo), 1922, 2, 328.

Diagnostic importance of glycosuria after injection of ADRENIN in pregnancy (Der diagnostische Wert der Adrenalinglykosurie für die Schwangerschaft). Küstner (H.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1340-1341.

During the first seven months of pregnancy 91% of all women have renal diabetes. To prove its existence the author recommends the so-called Brinnitzer-Roubitschek test. The patient takes on the empty stomach 10 gm. of glucose, dissolved in 150 to 200 cc. of water; twenty minutes later 0.5 mg. of adrenalin is injected subcutaneously. Blood sugar estimations are made before the test is begun and $\frac{1}{2}$, 1 and $1\frac{1}{2}$ hours after the injection. If after $1\frac{1}{2}$ hours no glucose is found in the urine, examination is made 2 and even 3 hours after the injection. Usually in $\frac{3}{4}$ to $1\frac{1}{2}$ hours sugar is found in the urine. The average maximum blood sugar is 0.140%.—J. K.

The ADRENALS in morphin intoxication (Suprarrenales o intoxicacion morfínica). Lewis (J. T.), Semana méd. (Buenos Aires), 1922, 29, 309-311 (August 10); cit., J. Am. M. Ass. (Chicago), 1922, 79, 2042.

(ADRENIN) Pharmacodynamic reactions of erectile tissue and the dorsalis penis artery. Macht (D. I.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 90-91.

Material from the dog was studied by methods devised by the author. The tissues studied responded to adrenin and ergotoxin but not to "parasympathetic" poisons. The author concludes that these tissues are innervated by the thoracico-lumbar sympathetic and not by the bulbo-sacral.—J. C. D.

The pharmacological and colorimetric determination of ADRENALIN in pure and decomposed solutions and ADRENAL extracts (Ueber die pharmakologische und Kolorimetrische Auswertung reiner und zersetzter Adrenalinlösungen sowie von Nebennierenauszügen). Maiweg (H.), *Biochem. Ztschr. (Berl.)*, 1922, 131, 292-300.

Folin's method for the determination of adrenalin gives too high values for solutions in which the compound is partially decomposed. Very inexact values are apparently given by the colorimetric method when applied to adrenal extracts. The content in adrenalin precursors gives rise to too high values. The pharmacological activity of adrenalin is not enhanced by oxidative decomposition.

—F. S. H.

Parabiosis with special reference to the transplantation and extirpation of the ADRENALS. Mayeda (T.), *Keio Igaku*, 1922, 2, No. 7; abst., *Jap. Med. World (Tokyo)*, 1922, 2, 330.

In successful parabiosis the removal of both adrenals in one of the "twins" does not result fatally. Separation of the parabiotics after 4 weeks may be made without death ensuing in either animal, accessory adrenals having had time to proliferate. Parabiosis of animals of different sex causes little or no change in the gonads.

—R. G. H.

Further data on the effect of SUPRARENAL insufficiency (by removal) in rabbits. Marine (D.) & Baumann (E. J.), *J. Metab. Research (Morristown)*, 1922, 2, 1-18.

The rabbit was chosen for the experiments because removal of its main suprarenal glands while leaving the small accessory cortical glands intact creates a condition of suprarenal insufficiency which is most desirable. The difficulties encountered in attempts to use other animals are pointed out. Eleven experiments are reported. The rate of heat production was determined before and after the production of adrenal insufficiency. Detailed protocols and tables illustrate the results. Careful histological study of the autopsy material was made. It was found that a prolonged absolute rise in heat production was obtained in 27 of 33 rabbits in which the two main suprarenal glands had been completely removed, and in 6 of 15 rabbits in which these glands were frozen with ethyl chloride. It was concluded that increased thermogenesis is due in part to an increased rate of discharge of the iodine-containing hormone from the thyroid, since thyroidectomy prevents this increased heat production. Infection, trauma, nerve injury, diet and muscular activity,

it was decided, are not essential factors in increased heat production.—I. M.

Further observations on the effect of SUPRARENAL insufficiency (by removal) in THYROIDECTOMIZED rabbits. Marine (D.) and Baumann (E. J.), *J. Metab. Research* (Morristown), 1922, 2, 777-802.

Almost total thyroidectomy was performed on rabbits which were then kept under standard conditions until thyroid deficiency was apparent. Epinephrectomy was then performed, with the production of sublethal suprarenal insufficiency. Respiratory exchange measurements, made with the modified Haldane open circuit apparatus at different intervals, indicated the absence of typical increase in heat production observed when the thyroid is present. It is concluded that there exists a thyroid-suprarenal cortex interrelationship which is separate from the thyroid chromophil tissue interrelationship. Evidence is pointed out that sufficient but sublethal suprarenal insufficiency in rabbits and in cats causes a rapid loss of iodine from the thyroid.—I. M.

Case of ADRENAL hemorrhage (Un cas d'hémorrhagie des surrénales). Mihcaux (J.) & Marsset (H.), *Bull. et mém. soc. méd. d. hôp. de Par.*, 1923, 47, 161-163.

An old man of 74 with profuse diarrhea and general fatigue died suddenly. At autopsy bilateral hemorrhage was found.

—F. S. H.

The influence of PANCREATIC infusion and pancreatic juice on ADRENALIN hyperglycemia. Murohashi (T.), Jikwa Zasshi, 1922, No. 266 (July); abst., *Jap. Med. World* (Tokyo), 1922, 2, 330.

The author employed infusions of cattle spleens, and in some cases noted an inhibition of experimental adrenin hyperglycemia; in other cases the infusions proved inactive. Protein-free pancreatic juice, boiled pancreatic infusion of cattle and of dog's pancreas all gave negative results.—R. G. H.

The influence of ADRENIN on the retina (Über den Einfluss des Adrenalins auf die Netzhaut). Nakamura (B.) & Miyake (R.), *Klin. Monatsbl. f. Augenh.*, 1922, 69, 258-266; abst., *Physiol. Abst. (Lond.)*, 1923, 7, 611.

Estimation of ADRENALINE in the blood. Okamoto (K.), *J. Bact. (Japan)*, 1921, No. 315; *Jap. Med. World* (Tokyo), 1922, 2, 88.

A modified Suto-Inouye method was used for the estimation of adrenaline in the suprarenal. To get rid of interfering substances, the author treated the serum with absolute alcohol and centrifuged at 3,000 r.p.m. for 20 minutes. He then added more $HgCl_2$ and

less Na acetate. He could demonstrate fairly accurately 0.00005 gm. of adrenaline in 5 cc. of the serum.—Physiol. Abst., 7, 586.

The action of ADRENALIN on the blood sugar (*Die Wirkung des Adrenalins auf den Blutzucker*). Petényi (G.) & Lax (H.), Biochem. Ztschr. (Berl.), 1921, 125, 272-282.

These experiments were done on children and infants. It was found that the preliminary hyperglycemia is followed by hypoglycemia; that the variability of the blood sugar in tetany is greater than normal; that the administration of adrenalin in patients with tetany is followed by a hyperglycemia of lesser degree than normal and that hypoglycemia does not appear.—F. S. H.

An intervening mechanism in the fixation of fat by the ADRENAL gland (*Sur un mécanisme intervenant dans la fixation des graisses par la glande cortico-surrénale*). Pollicard (A.) & Tritchkovitch (Juliana), Compt. rend. Acad. d. sc. (Par.), 1922, 174, 960-961.

ADRENALIN in the incoercible vomiting of pregnancy (*L'adrénaline dans les vomissements incoercibles de la grossesse*). Rathery, Gynéc. (Par.), 1922, 24, 614-615.

Report of 4 cases. The drug was administered either subcutaneously (1 mg. of the hydrochloride in 250 cc. physiological saline) or by ingestion (1 or 2 mg.) or by lavage (1 mg.) for from 2 to 7 days. The results were immediate; vomiting stopped in 24 to 48 hours; acidosis disappeared in 3 or 4 days and weight increased. Relief was permanent. —F. S. H.

Some effect of EPINEPHRIN on the heart of the common bull-frog (*Rana catesbiana*). Reed (C. I.) & Smith (Erma), Am. J. Physiol. (Balt.), 1923, 63, 566-582.—T. C. B.

Effects of ADRENALIN and extracts of PANCREAS and LIVER on blood dextrose. Ross (E. L.) & Davis (L. H.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, 20, 121-128.

Experiments were conducted on dogs. Intravenous injection of 0.25 cc. of a 1-1000 solution of adrenalin per kilo produced an increase of 62% in the blood sugar at the end of 15 minutes. This fell to 31% at the end of an hour. Fresh pancreatic extract brought about a decrease in four out of five trials. This decrease averaged 23% at the end of 15 minutes and had fallen to 5% after one hour. Pancreas extract injection, followed at once by injection of adrenalin, gave an increase of 39% 15 minutes after the injections. This fell to 9% at the end of one hour. The results obtained from injection of a mixture of the pancreas extract and adrenalin after incubation for 30 minutes were not constant. The injections were controlled by injection of liver extract and of liver extract followed by adrenalin. The extract of liver gave small increases in glycemia, while

parts—whole blood, plasma and corpuscles—for total fat, lecithin and cholesterol. Apart from a sufficient supply of fat in the diet, the one indispensable prerequisite for diabetic lipemia was found to be the existence of active severe symptoms in the form of glycosuria and hyperglycemia. Mild cases with high glycosuria and severe cases with glycosuria abolished by diet were found never to exhibit extreme lipemia, however high the fat intake. It was concluded that diabetic lipemia represents some secondary breakdown in fat metabolism, not directly connected with the endocrine function of the pancreas and not due merely to excess of fat in metabolism or loss of sugar in the urine. It was found that there are wide individual variations in susceptibility to lipemia. Tests under all of the endocrine, dietary, drug and other influences listed failed to reveal the exact nature of the disturbance or the origin of susceptibility to lipemia.—I. M.

Observations on the progressiveness of DIABETES. Allen (F. M.), Med. Clin. N. Am. (Phila.), 1922, 6, 465-474.

This is an important discourse dealing with probable causal relationships upon which the course and prognosis of diabetes mellitus depend. The avoidance not only of glycosuria but of hyperglycemia is the means of curbing the downward progress of the patient. The function of the islands of Langerhans is impaired by infection and intoxication; this leads to the usual diabetic symptoms, rendering the pancreas highly susceptible to functional overstrain. Case histories exemplify the contrast between patients treated with a diet restricted to overcome functional strain and those treated with a high diet in the fallacious attempt to "build up" the patient. There appears to be no mysterious element to account for the progressiveness of diabetes mellitus, but only infections and functional overstrain. It is urged that in the physical examination of students in schools and colleges, urinalysis be included in order promptly to detect and treat early cases of the disease. Moreover, since there is no valid distinction between true diabetes and other forms of glycosuria with hyperglycemia, even the mildest cases of the former are susceptible to aggravation from functional overstrain.—I. B.

Present status of DIABETIC treatment. Allen (F. M.), N. Jersey M. Soc. J. (Orange), 1923, 30, 1-15; cit., J. Am. M. Ass. (Chicago), 1923, 80, 657.

Changes in the chemical composition of the blood in health and DIABETES after ingestion of salt solutions (Über Aenderungen der chemischen Zusammensetzung des Blutes nach dem Trinken von Salzlösungen bei Stoffwechselgesunden und Zuckerkranken). Arnoldi (W.) & Ettinger (S.), Klin. Wchnschr. (Berl.), 1922, 1, 2082-2083.

The authors studied the effect of warm water, solutions of Karlsbad salt, Na_2SO_4 , citrate of sodium and bicarbonate of sodium on the blood sugar, the amount of NaCl and proteins in the blood, and the alveolar CO_2 tension in arterial blood. The blood sugar usually showed a decrease, which was much more marked in diabetes than in health. NaCl change was not constant; normal persons generally showed an increase, while diabetics usually showed a decrease. The CO_2 tension and the protein content of the serum were in nearly all cases lowered.—J. K.

Some chemical reactions of INSULIN. Best (C. H.) & Macleod (J. J. R.), J. Biol. Chem. (Balt.), 1923, 55, xxix-xxx; see also, Am. J. Physiol. (Balt.), 1923, 63, 390 (Proc.).

Insulin from pancreas of ox or pig gives the usual protein reactions. That from the skate does not. The former is due to protein impurities. Insulin does not give the usual color reactions for epinephrin. Moderate heat does not affect the reactivity in faintly acid reaction. Moderate alkalinity is also harmless for short periods. Insulin in acid is adsorbed by charcoal, etc. Insulin apparently does not dialyze and is weakened by the dialyzer. The potency of insulin preparations may be weakened by passing through a Berkfeld filter.—F. S. H.

Influence of certain carbohydrate diets on glycemia in man, normal or DIABETIC (Influence de certains aliments hydrocarbonés sur la glycémie de l'homme normal ou diabétique). Bonorino Udaondo (C.) & Casteigts (M.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 392-393.—T. C. B.

DIABETIC gangrene of the scrotum and integuments of the penis: antigangrenous scrotherapy: cure (Gangrène diabétique du scrotum et des téguments de la verge. Sérothérapie antigangreneuse. Guérison). Chauffard (A.), Huber (J.) and Marquézy (R.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 270-273.

The influence of PANCREATIC perfusates on the blood sugar, D:N ratio and respiratory quotient of depancreatized animals. Clough (H. D.), Stokes (A. M.), Gibbs (C. B. F.), Stone (N. C.) & Murlin (J. R.), J. Biol. Chem. (Balt.), 1923, 55, xxx-xxxi.

Perfusion of the pancreas of the dog, pig and cow, by Clarke's method, withdraws the antidiabetic substance in sufficient concentration to affect favorably all the major symptoms of diabetes produced by depancreatization. In several instances the blood sugar was reduced to normal or lower by a single injection; the excretion of sugar was stopped by 2 or 3 injections. When the perfusion fluid is made slightly acid more potent extracts are obtained. The name glucopyron is suggested for the effective extracts obtained from the pancreas.—F. S. H.

The occurrence of ketone bodies in the urine of normal rabbits in a condition of hypoglycemia following the administration of INSULIN—a condition of acute acidosis experimentally produced. Collip (J. B.), J. Biol. Chem. (Balt.), 1923, 55, xxxviii-xxxix.

While we have in insulin a substance which will correct all the acidotic signs, both in experimental animals rendered diabetic and in patients suffering from diabetes (if the dosage is adequate), it will nevertheless produce many of the cardinal symptoms of acidosis when administered to normal animals in amount sufficient to produce hypoglycemia of a marked degree.—F. S. H.

The demonstration of an insulin-like substance in the tissues of the clam (*Mya arenaria*). Collip (J. B.), J. Biol. Chem. (Balt.), 1923, 55, xxxix.

Since insulin aids in the storage of glycogen in the dog, it might be expected that wherever glycogen occurs there would be insulin. A substance acting somewhat similar to insulin was extracted from the tissues of the clam.—F. S. H.

The original method as used for the isolation of INSULIN in semi-pure form for the treatment of the first clinical cases. Collip (J. B.), J. Biol. Chem. (Balt.), 1923, 55, xl-xli.

Of great historical interest.—F. S. H.

Delayed manifestations of the physiological effects of INSULIN following the administration of certain pancreatic extracts. Collip (J. B.), Am. J. Physiol. (Balt.), 1923, 63, 391-392 (Proc.).

Certain extracts produce no immediate hypoglycemia. One to four days after inoculation, however, animals may show hypoglycemia. It would seem that insulin does not exist as such in any quantity in the islet cells. The potency of the extract is due to the method of extraction used, and suggests that a mother substance is activated by certain reagents. In delayed action the mother substance is present and is gradually activated after injection.—T. C. B.

DIABETE et acidose. Desgrez (A.), Bierry (H.) & Rathery (F.), Compt. rend. Soc. de biol. (Par.), 1922, 86, 245-247.

These authors take the view that in certain conditions metabolic disturbances can only be avoided by a definite relationship in the amounts of protein, fat and carbohydrate in the diet. They have investigated the diabetic from this point of view. They divide diabetics into: (1) those who eliminate acetone bodies regularly in large amounts; (2) those who eliminate them intermittently; and (3) those whose urinary N is high. A determination is first made of the sugar and acetone bodies excreted after 2 days in which only water is taken. They find that for each patient a diet can be determined containing protein, fat and carbohydrate in a ratio peculiar

for the patient, on which the excretion of acetone bodies is as low as when fasting.—Physiol. Abst., 7, 121.

DIABETIC acidosis. Desgrez (A.), Bierry (H.) & Rathery (F.), Bull. Acad. de méd. (Par.), 1923, 80, 25-33; abst., J. Am. M. Ass. (Chicago), 1923, 80, 805.

Some properties of an active constituent of the PANCREAS (INSULIN). Dolsy (E. A.), Somogyi (M.) & Shaffer (P. A.), J. Biol. Chem. (Balt.), 1923, 55, xxxi-xxxii.

Insulin has been prepared by methods of Collip, Banting and Best. Purification reached the point in which about 0.25 mg. of material produced hypoglycemia in rabbits of 1 kilo weight. It is a white powder containing 14% nitrogen. It is free from phosphorus. It gives a distinct biuret test. Its solutions are levorotary. It is acid resistant. It is soluble in water except at pH 5-6. It is fairly soluble in alcohol. It is pretty well precipitated by half saturated ammonium sulfate. It appears to be an albumose or globulin. The identity is not established. The method of preparation is given.—F. S. H.

Experimental DIABETE gras. Friedman (G. A.) & Gottesman (J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1923, 20, 210-212.

In 8 dogs the authors demonstrated that diabetes with obesity can be produced: (1) "by almost complete thyroidectomy in partially depancreatized dogs," and (2) "by ligation of one pancreatic duct."—J. C. D.

Influence on the respiratory metabolism of PANCREATIC extract administered by mouth to depancreatized dogs. Gibbs (C. B. E.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 198.

There was an elevation of the respiratory quotient when measured 2 to 4 hours after such administration. The methods of preparation and the tabulated result of one experiment are included.

—J. C. D.

An atypical adenoma of the PANCREAS originating in islet tissue. Goldblatt (H.), J. Cancer Research (Balt.), 1921, 6, 277-283.

Report of a case the pathology of which is sufficiently described in the title. There was no apparent disturbance of carbohydrate metabolism.—J. P. S.

Plea for testing selected single specimens of urine, with special regard to DIABETES. Gray (H.), Boston M. & S. J., 1923, 188, 168; abst., J. Am. M. Ass. (Chicago), 1923, 80, 800.

The effect of Eck's fistula upon PANCREATIC DIABETES in dogs. Hendrix (B. M.) & Sweet (J. E.), J. Biol. Chem. (Balt.), 1923, 55, 161-169.

It has been shown that glucose practically disappears from the urine of Eck's fistula pancreatectomized dogs after they have fasted for several days. There is, however, definite hyperglycemia in such animals even after prolonged fasting. The alkali reserve in the blood of these dogs does not decrease so rapidly as after simple pancreatectomy and the ability to utilize sugar is very slight. It is suggested that little glucose is formed from amino-acids in Eck's fistula dogs.—F. S. H.

DIABETES MELLITUS. Herndon (R. F.), Illinois M. J. (Oak Park), 1923, 43, 137-144.

A good survey of the etiology and treatment of diabetes mellitus. The importance of diet in treatment is emphasized.—I. B.

Observations in DIABETES (Beobachtungen bei Diabetes). Höpfner (H.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1284-1285.

In diabetes exposure of the liver to x-rays did not change the blood sugar; x-ray treatment of the adrenals first produced a rise of the blood sugar, followed by a temporary fall. When bone marrow was exposed to x-rays no influence on sugar in the blood or urine was seen. Administration of antithyroidin in diabetes had no influence upon the glycosuria. Bone charcoal or bolus alba did not change the glycosuria nor produce an increase in the quantity of sugar, acetone and diacetic acid in the urine.—J. K.

(PANCREAS) The islands of Langerhans in the skate. Jackson (S.), J. Metab. Research (Morristown), 1922, 2, 141-147.

By the use of Lane's method for identifying islet tissue with Bensley's neutral gentian stain for differentiation of alpha and beta cells, the author has studied the structure of the pancreatic tissue in the skate. The islets stand out as less deeply stained areas surrounding the pancreatic ducts. In each islet there are seen the larger alpha cells with deeply staining granules and the more numerous smaller beta cells, the cytoplasm of which is clear. No definite "transitional cells" were seen, a fact which makes it improbable that acinar cells are converted into islet cells as has been claimed.—I. M.

(DIABETES) The interpretation of blood sugar estimations that are near the normal. John (H. J.), J. Lab. & Clin. M. (St. Louis), 1922, 8, 145-152.

The author points out in a series of cases that we cannot regard a blood sugar level which is near the normal as normal unless we know under what conditions it was obtained (i. e., whether the subject is on a diet or has been eating sparingly for a time) and unless we can demonstrate by a glucose tolerance test that the slight rise is of nondiabetic origin. Border-line cases are the most difficult to diagnose and yet the most interesting and important. When

it is seen that the border-line subject has a diabetic trend, a simple restriction of carbohydrates will carry him through life comfortably. Usually the total calories need not be changed. On the other hand, if such a case is allowed to drift along without dietary supervision, he will reach the stage of diabetes when a marked restriction of proteins and total calories, as well as carbohydrates, will be necessary.—I. B.

(DIABETES) The excretion of sugar in the urine in health and disease. Kast (L.), Croll (Hilda M.) & Myers (V. C.), J. Lab. & Clin. M. (St. Louis), 1923, 8, 227-241.

In a comparative study of different methods for the determination of sugar in normal urine, the authors conclude that by the method of Benedict and Osterberg there is shown to be an increase in the amount of reducing sugar excreted hourly after meals. A diet rich in carbohydrates produces an increase in the sugar excreted, as compared to a low carbohydrate diet. In the 152 cases studied, there were no marked variations from the normal sugar excretion on ordinary diets, except in cases of diabetes mellitus. Moreover, when by dietary regulation the urine is rendered "sugar free," the daily amount of sugar excreted is practically normal.
—I. B.

New ideas on, and treatment of, DIABETES MELLITUS (Neue Auffassung und Behandlung des Diabetes mellitus). Klieneberger (C.), Klin. Wehnschr. (Berl.), 1922, 1, 1630.

The war brought out the fact that traumatic diabetes is very rare. Excretion of sugar after infectious diseases is not so rare. There is danger of protein over-feeding. The author believes that individualized treatment is necessary, but that the severe therapy advocated by Geulpa or Allen is unsatisfactory.—J. K.

Soya bean flour in treatment of DIABETES MELLITUS. Jones (C. B.), Med. Sentinel (Portland, Ore.), 1921, 29, 422-424.

Jones believes that soya beans tend to eliminate the craving for carbohydrate in the diabetic subject and to provide a non-carbohydrate food of great value.—M. B. G.

Examination and medical surveillance of the DIABETIC (Examen et surveillance médicale d'un diabétique). Labbé (M.) & Bith (H.), J. de méd. de Par., 1921, 40, 349-350.

Further experiments with high fat diets in DIABETES. Leclercq (F. S.), J. Metab. Research (Morristown), 1922, 2, 39-55.

Three cases of diabetes are reported in full which confirm the author's previous conclusions that high fat diets are harmful in that they overstrain the function of the carbohydrate mechanism as well as cause ketonuria. The value of undernutrition by diets which keep the blood sugar near the normal level is emphasized.—I. M.

Physical measurements of DIABETIC patients. Root (H. F.) & Miles (W. R.), *J. Metab. Research* (Morristown), 1922, 2, 173-197.

From a study of 133 diabetic patients the authors found that although normal in stature the subjects had been on the average 20% overweight prior to onset and were about 10% underweight at the time of examination. The 56 women showed more severe diabetes and lower carbohydrate tolerance than the 77 men observed. The older patients had been more obese and had lost a larger percentage of their weight. The type of diabetics who apparently had never been overweight had the narrow type of chest and probably had been fat for their build. Obesity was found to be closely related to the onset of diabetes mellitus, but the intensity of the disease frequently appeared to be inversely proportional to the amount of excess fat. Chest circumference was not found to be a satisfactory measure for predicting normal weight. Vital capacity may be as great in diabetic as in normal subjects and is, therefore, not of any help in uncomplicated diabetes.—I. M.

Normal, DIABETIC and Basedowian alimentary hyperglycemia (Blood sugar studies) [Die alimentäre Hyperglykämie bei Gesunden, Diabetikern und Basedowischen (Blutzuckerstudien)]. Rosenberg (M.), *Arch. f. exper. Path. u. Pharmakol.* (Leipz.), 1922, 93, 208-240.

Experiments with 100 gm. dextrose dissolved in 300 cc. caffeineless coffee substitute, which was given 2 hours after the first breakfast. The blood sugar was examined first on the empty stomach and thereafter at about half-hour intervals for 2 hours. Duration of intestinal resorption may be considered as constant and has no important influence upon the blood sugar curve. The sudden rise of the blood sugar curve may be caused by decreased carbohydrate assimilation in the liver or by increased consumption. The duration of hyperglycemia depends not only on the duration of influx from the liver, but also on the amount of sugar absorbed by the muscles. The curve usually reaches a maximum in normal subjects $\frac{1}{2}$ hour after excretion of the dextrose. The increase averages 0.1%. After 2 hours the blood sugar is usually normal. In diabetics hyperglycemia is increased, continues longer, and reaches the maximum later than in normal subjects. The author especially emphasizes this last fact; he finds a certain parallelism between the gravity of the diabetes and the time the maximum is reached. Most diabetics reach the maximum in 1.5 to 2 hours. The author believes that in diabetes the liver forms sugar more easily, the sugar forming activity being greatest shortly after ingestion because its stimulating effect is gradually increasing. He states that possibly the ability to form glycogen in the tissues, especially in the muscles, diminishes simultaneously. Three cases of renal diabetes

showed a normal hyperglycemia curve after dextrose ingestion, but measurable sugar in the urine. In case of Graves' disease the curves are not regular—in several cases being normal, in others resembling the diabetic curve. The pathological alteration of the curve is not parallel to the gravity of clinical symptoms of hyperthyroidism. Sugar excretion from the liver seems to be increased in these subjects also.—A. B.

(DIABETES) The progress of potentially DIABETIC persons in relation to dietary control. Sherrill (J. W.), *Med. Clin. N. Am.* (Phila.), 1922, 6, 719-737.

A report of the result of the treatment of a series of cases of supposed latent or potential diabetes. It is pointed out that tolerance is decreased with prolonged overnutrition and gradual rise in body weight. On the other hand, persons with proved tendency to lowered glucose tolerance, but without frank diabetic manifestations, improve in carbohydrate assimilation following application of the principle of low nutrition.—I. B.

Balancing the DIABETIC diet. Strouse (S.), *J. Am. M. Ass.* (Chicago), 1922, 79, 1899-1900.

A line of treatment for diabetes which seeks to avoid the starvation methods of Allen and Graham is that in which a proper proportion of fat is administered. This paper gives rules for determining quickly the right amounts of protein, fat, and carbohydrate appropriate to a given case. The basal metabolism is first determined, and the total caloric value of the food should approximate to this. The protein should be the minimum amount compatible with nitrogen equilibrium, which is given as 0.66 gm. per kilo of body weight. The carbohydrate content should be that amount which can be tolerated (this to be determined during 2 days on a fixed diet; it is the intake less the amount in the urine), subtracting from this tolerated amount 58% of the protein. The rest of the caloric requirement should be fat, though this must be within limits 2.5-4.0 times the available carbohydrates, otherwise there will be ketonuria.—*Physiol. Abst.*, 7, 610.

Dinitrosalicylic acid; A reagent for the estimation of sugar in normal and DIABETIC urine. Sumner (J. B.), *J. Biol. Chem.* (Balt.), 1921, 47, 5-9.

A new colorimetric method.—F. S. H.

DIABETES in old age (Contribution à l'étude du diabète sucré chez le gens âgés. Yeanty (A. y R.), Thèse pour le Doctorat en Médecine, Bordeaux, 1922.

Diabetes is rarely seen in a subject over 60 years of age. In an old person the symptoms are weakened. Nutritional disorders,

albuminuria, rheumatism, gout, asthma, obesity, and eczema are often associated with diabetes.—E. G.

Post-traumatic calcification of the PANCREAS, with DIABETES.

Wells (H. G.), Tr. Chicago Path. Soc., 1922, xi, 255-256; in full, Am. J. Med. Sc. (Phila.), 1922, 164, 474-492.

This report concerns a "previously healthy young man who fell from a wagon and was probably run over by at least one of the wheels. He received fractures of several ribs on the left side, traumatic infarction of the left adrenal, the upper pole of the spleen, and the entire left kidney, together with a crushing injury of the pancreas which resulted in complete destruction of the secreting elements, which were replaced by a large quantity of dense fibrous tissue and extensive deposits of calcium salts." The urine in the bladder at necropsy contained sugar. "A review of the literature has failed to reveal a similar case of extensive pancreatic calcification, or an analogous case of diabetes following crushing injury of the pancreas."—J. P. S.

Disseminated sclerosis as a cause of myopia and DIABETES (La esclerosis diseminada como causa de la miopia deletera y de la diabetes). Wernicke (O.), Semana méd. (Buenos Aires), 1921, 28, 97-105.

The author believes that specific spirochetosis produces sclerosis "en plaques," retinal detachment, severe myopia, chronic rheumatism, serious incretory disorders and diabetes.—B. A. H.

Analyses of blood lipoids in DIABETIC animals and patients.

Wishart (M. B.), J. Metab. Research (Morristown), 1922, 2, 199-217.

A partial report of an extensive study on lipemia. Careful observations on the cholesterol, lecithin, total fat, fatty acids, glycerids, blood and urine sugar and acetone and plasma CO₂ were made in diabetic dogs and patients under varying conditions. Diets were varied as regards the relative proportions of fat, protein, carbohydrate, alcohol and total caloric value. Observations were made before and at intervals after ingestion of cholesterol and lecithin. It was found that marked lipemia is due chiefly to increase in neutral fat. The higher the degree of lipemia, the higher is the ratio of glycerids to other lipoids such as lecithin and cholesterol. Total fats may be very high with a clear plasma, and marked turbidity may be present without marked hyperlipemia. Some degree of lipemia may persist long after hyperglycemia, glycosuria and acidosis have disappeared in severe cases. Cholesterol or lecithin feeding have no decisive influence in either producing or clearing up lipemia. No uniform parallelism was observed between the sugar or acetone in blood or urine and the accompanying degree of lipemia.—I. M.

Microphotographs of a case of **DIABETES INSIPIDUS**. Lewy (F. H.), *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1663.

Demonstrations of microphotographs, proving that diabetes insipidus is due to changes in the ganglion parhypophysis, situated in the tuber cinereum.—J. K.

Case of **DIABETES INSIPIDUS** successfully treated by **PITUITARY** extract. Reece, J. *Missouri M. Ass. (St. Louis)*, 1921, 18, 463.

When admitted to the metabolism ward the patient's fluid intake and output ranged from 12 to 15 liters and could not be reduced below 7 liters. Adrenalin by mouth and duodenal tube was without effect. Desiccated pituitary extract, posterior lobe, was given by mouth in salol-covered capsules, the dose being $\frac{1}{2}$ gr., t. i. d. at first, and increasing gradually to 4 gr. four times a day. Intramuscular injection of pituitary fluid was also effective, but desiccated extract in powder form was not successful when given by mouth or rectum.—M. M. H.

Neurologic phase of **ENDOCRINOLOGY**. Bitler (C. C.), *Indiana State M. Ass. J. (Ft. Wayne)*, 1922, 15, 414-423.

See *Endocrin.*, 7, 130.

(**ENDOCRINE**) The character and the cause of Paget's osteitis deformans (*Zur Frage des Wesens und der Pathogenese der Ostitis deformans Paget*). Caan (P.), *Beitr. z. klin. Chir. (Tübing.)*, 1922, 125, 212-244.

This is considered by some investigators as an endocrine disease and many cases are reported in which changes in the endocrine organs have been found at autopsy. Askanazy found pathological changes in the thyroid; Meyer and Schmorl found very large parathyroids; in a case of Recklinghausen's disease there was a basophil adenoma of the hypophysis without other symptoms. Caan advances a new theory as follows. The disease begins with endocrine disturbances; pathological hormones are produced and cause inflammation of the bone marrow, followed by hyperplasia and hemorrhages. Heredity predisposition probably has a rôle. In some cases organotherapy is reported to have been unsuccessful; in others, thyroid extract seemed to bring about good results.—J. K.

Stiffness of the vertebral column and **ENDOCRINE** disturbance (*Wirbelsäulenversteifung und Störungen der innere Sekretion*). Cohn-Wolpe (C.), *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1505-1507.

Report of a case. The vertebral column was exceedingly stiff. There were also very marked symptoms of thyrogenous origin (exophthalmus; positive Moebius, Stellwag and Grafe symptoms; no goiter). The skin of the trunk, and especially in the axillae and groins, showed dark pigmentation. The mucous membrane, how-

ever, was not pigmented. A few references from the literature concerning diseases of the joints and endocrine symptoms are quoted. The author discusses whether the patient suffered from Addison's disease, but the symptoms which would be of special importance, such as blood pressure, sugar tolerance and ergographic findings, are not mentioned.—J. K.

(ENDOCRINE) Sclerodermic dystrophy (Ueber sklerodermische Dystrophien). Curschmann (H.), *Med. Klin. (Berl.)*, 1921, 17; 1223-1225; abst., *Schweiz. med. Wchnschr. (Basel)*, 1923, 53, 132.

A 42 year old emaciated invalid showed, along with sclerodactylia, thyroid deficiency, impotence, marked pigmentation, adynamia, hypotonia and eosinophilia. The author believes that this indicates that pluriglandular insufficiency is the etiologic factor. He includes the skin among the incretory organs involved.—R. G. H.

Diagnosis of disorders of the DUCTLESS GLANDS. Engelbach (W.), *Northwest Med. (Seattle)*, 1922, 21, 348-351.

Brief report of a lecture, elaborately illustrated by lantern slides, of patients showing striking examples of various types of endocrine diseases.—H. L.

Pluriglandular ENDOCRINE insufficiency (Beitrag zur Klinik der pluriglandulären endokrinen Insuffizienz). Frisch (A.), *Med. Klin. (Berl.)*, 1921, 17, 1021-1023; abst., *Schweiz. med. Wchnschr. (Basel)*, 1923, 53, 126.

A case report—interesting in that the beginning of the disorder coincided with a febrile disease.—R. G. H.

Surgical aspects of ENDOCRINOLOGY. Gatch (W. D.), *Indiana State M. Ass. J. (Ft. Wayne)*, 1922, 15, 423-430.

See *Endocrin.*, 7, 138.

Mental diseases and the ENDOCRINE sympathetic system (Le malattie mentali in rapporto alla patologia dell' a parecchio endocrinosimpatico). Goldstein (L.), *Endocrin. e patol. costituz. (Roma)*, 1922, 1, 17-36.

Theoretical, applying Pende's conceptions to psychiatry.—G. V.

An investigation of the basal metabolism in unstable conditions of certain ENDOCRINE glands. Hill (H. G.), *Quart. J. Med. (Oxford)*, 1922, 15, 331-347.

Hill studied the basal metabolism, by the Douglas bag method [as described by Cathcart, *J. Roy. Army Med. Corps (Lond.)*, 1918, 31, 339] in 33 patients presenting symptoms ascribed to disorders of one or more of the ductless glands. The results of Hill's estimations of basal metabolism in gross disorders of the thyroid gland "agree with those of other observers, and indicate the great value

of this method of examination in estimating the degree of glandular activity prevailing at the time of observation." In "gross disorders" of the pituitary gland, Hill found a marked increase of basal metabolism in two out of three cases of acromegaly; a basal metabolic rate of plus 37.7% in one patient with dyspituitarism; and in hypopituitarism, rates ranging from -6.7% to -33.3%. These results "have proved of value in the diagnosis and treatment" of conditions associated with derangements of the hypophysis. Estimations of the basal metabolism at the physiological epochs of life in subjects, especially women, who show any tendency to thyroid or pituitary instability, "are of great value in confirming any early abnormality, and indicate lines for suitable treatment." Hill considers that he has established the value of basal metabolism estimations in children suffering from nocturnal enuresis. "An indication is obtained as to those likely to derive benefit from treatment with glandular extracts." Most of these patients showed a low metabolic rate, and improved under thyroid extract. In an investigation of patients suffering from phenomena which are apparently due to parasympathetic overexcitability "a group of cases has been isolated showing a subnormal basal metabolic rate." Several of these patients showed nocturnal enuresis. They "benefit greatly from organotherapy."—J. P. S.

(ENDOCRINE) Indisposition and cachexia by x-rays (Ueber Röntgenkaker und Kachexie). Hirsch (H.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1646-1647.

The author believes that the disagreeable sensations felt after x-ray treatment are partially related to the endocrine system. Since endocrine gland extract has been administered the disagreeable symptoms are scarcely ever observed, even in subjects exposed to very large doses of x-rays.—J. K.

(ENDOCRINE) Organ weights in albino rats with experimental rickets. Jackson (C. M.) & Carleton (Rachel), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 20, 181.

Fifty-four rats were used. The degree of rickets varied as shown by the skeleton. There was an increase in the weight of the adrenals; a decrease in the weight of the hypophysis and especially of the thymus; and no change in the spleen, ovaries, testes and epididymus.—J. C. D.

(ENDOCRINE) Acrodermatitis atrophicans with scleroderma "en plaques." Jadassohn, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1663-1664.

A short note. Both symptoms are of endocrine origin.—J. K.

(ENDOCRINE.) An isolated disturbance of salt metabolism as a symptom of a disease of the interbrain (Ueber eine isolierte

Störung des Salzstoffwechsels als Symptom einer Erkrankung des Zwischenhirns). Jungmann (P.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1297; see also, Klin. Wchnschr. (Berl.), 1922, 1, 1546-1548.

A man of 28 without diseases of the heart or kidneys complained of general dropsy with pluriglandular endocrine symptoms. A radiogram of the skull showed important changes in the sella. The blood contained much water and a low quantity of NaCl. The excretion of NaCl was very defective. Theocin or thyroidin increased the excretion of NaCl; pituitrin had no influence. The author believes this disease to be localized in the interbrain. No other details are given.—J. K.

(ENDOCRINE) The principles underlying the treatment of the diarrheas. Kantor (J. L.), Med. Clin. N. Am. (Phila.), 1922, 6, 569-570.

A general review of treatment of diarrhea, including diarrhea due to Addison's disease and Basedow's disease. The diarrhea of these latter is sudden in onset, the stools are watery and contain mucus and bilirubin, and the attacks may end as abruptly as they come. Treatment is successfully accomplished by rectal injections of 25 to 30 drops of a 1-1000 solution of adrenalin chloride in 200 to 300 cc. of water. Such an enema may be repeated several times a day, as adrenalin by intestine produces no systemic effects. One injection, however, is usually sufficient, as no stools are passed from 15 to 24 hours following the treatment. The author quotes Shapiro and Marine, who have had good results from the use of a glycerin extract of suprarenal cortex by mouth in the alleviation of diarrhea and other symptoms of Graves' disease. In the treatment of diarrhea of pancreatic obstruction, the administration of pancreatic extract or of fresh pancreas is of service.—I. B.

(ENDOCRINE) A case of mammary adenocarcinoma with peculiar relation to the glands of internal secretion. Klemperer (P.), Tr. Chicago Path. Soc., 1922, 11, 295-297.

Brief report of adenocarcinoma of the mammary gland with extensive metastases in the bones. Three of the parathyroid bodies were normal in size and shape; the left inferior body was replaced by a tumor measuring 30 by 5 by 3 mm., entirely separated from the thyroid gland. Histologic examination revealed both chief and eosinophile parathyroid cells. The former were arranged mostly in cords, partly, however, as alveoli. The latter were accumulated in relatively large groups, one group harboring a small cancer metastasis. The fact that the tumor was composed equally of both kinds of normal parathyroid cells indicated that it was a hyperplasia. Klemperer is of the opinion that this hyperplasia was the result of the destruction of bone by the cancer metastases. He doubts, how-

ever, whether this represents a hyperfunction, because the osteoid tissue about the metastases did not show any trace of calcification. There was also a metastasis in the posterior lobe of the hypophysis which entirely destroyed this structure. The patient did not show the symptoms of diabetes insipidus, a fact which, he thinks, corroborates the view that the neural portion of the hypophysis does not regulate the secretion of urine.—J. P. S.

Questions of metabolism and INTERNAL SECRETIONS during and after pregnancy (Stoffwechselfragen und innere Sekretion in und nach der Schwangerschaft). Knipping (H. W.), Arch. f. Gynäk. (Berl.), 1922, 110, 520-534.

The contention of Zangemeister that there occurs a terminal physiological weight increase in pregnancy is substantiated. This is accompanied by a typical change in the respiratory metabolism and is considered as due to certain changes in the function of the anterior lobe of the hypophysis. Metabolic and clinical studies show to Knipping that the adiposity of the climacteric is of hypophyseal origin rather than due to ovarian involution.—F. S. H.

(ENDOCRINE) Fatal epilepsy in a GOITROUS woman recently OVARIECTOMIZED. HYPOPHYSEAL hemorrhage. (Etat de mal épileptique mortel chez une femme goitreuse récemment ovariectomisée. Hémorragie de l'hypophyse). Marchand (L.) & Adam (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1923, 47, 168-172.

The patient showed also neuro-muscular asthenia, crises, disturbances of memory, and facial congestion.—F. S. H.

ENDOCRINE therapeutics in osteomalacia (L'endocrinologia nell'osteomalacia agli intenti terapeutici. Marniucci (C. P.), Arch. di ostet. e ginec. (Napoli), 1923, 17, 26-33.

A review.—R. G. H.

ENDOCRINOLOGY in its medical aspects. McCaskey (G. W.), Indiana State M. Ass. J. (Ft. Wayne), 1922, 15, 409-414.

See Endocrin., 7, 143.

(ENDOCRINE) Some points in metabolism usually neglected by the physician. McClendon (J. F.), J. Lab. & Clin. M. (St. Louis), 1922, 8, 194-196.

Of interest to the laboratory technician and must be read in its entirety to be appreciated.—I. B.

INTERNAL SECRETION and dermal affections. Matsumoto (S.), Hifuka Hitsunyokikwa Zasshi, 1922, 22, No. 6 (June); cit., Jap. Med. World (Tokyo), 1922, 2, 333.

(ENDOCRINE) The relation between INTERNAL SECRETION and fat and lipoids occurring in blood. Okada (Y.), *Igaku Chyuo Zasshi*, 1922, 19, No. 24 (June); abst., *Jap. Med. World* (Tokyo), 1922, 2, 324.

Fatty acid, cholesterin and lecithin of the whole blood, erythrocytes and plasma increase and decrease in parallel with one another. The Europeans have a little higher concentration of these fatty substances than the Japanese. In Basedow's disease, fatty acid and cholesterin contents seem to decrease in the whole blood and plasma. The injection of thyroid preparation is followed by a slight augmentation of these substances, due to intoxication, but after internal administration of small doses a decrease due to augmented metabolism would be the result. The increase which is met with after the extirpation of the thyroid may be explained by the derangement of metabolism, and injection of thyroid preparation to the thyroidectomized animal would result in decrease. Adrenalin injection results in a remarkable increase of these substances. Pituitrin may also bring about a less notable increase. Genital gland feeding causes decrease, which may be due to the increased metabolism.—R. G. H.

Hematologic pictures in endocrine syndromes found associated with epilepsy. Patterson (H. A.), *Am. J. Psychiat.*, 1923, 2, 427-437 (January).

A study of the blood of 123 cases of endocrine disorders in epileptics. Both hyperthyroid cases (6) and hypothyroid cases (6) showed a mononucleosis—the hyperthyroid cases showing an increase of the transitional groups. Hyperpituitary cases (14) showed lymphocytosis and the hypopituitary cases (85) showed eosinophilia and mononucleosis.—F. H. A.

Demonstration of some ENDOCRINE cases (*Demonstration einiger Fälle von endokriner Funktionsstörung*). Petschacher, *Wien. klin. Wchnschr.*, 1922, 35, 749; see also, *Klin. Wchnschr. (Berl.)*, 1922, 1, 1628.

A demonstration of a eunuchoid of adipose type; a eunuchoid of tall type; twins of 14, having enuresis, a myxedematous habitus, small sexual organs, and swollen spots on the hands and legs; a "forme fruste" of myxedema with normal sexual organs, but without sexual desires and with defective bone formation; and brothers of 4 years, both of whom have goiters, without myxedema, and without sexual desires. In all these cases it is impossible to find the particular organ which causes these symptoms, since all endocrine diseases are pluriglandular.—J. K.

(ENDOCRINE) Constitutional factors in cancer and tuberculosis (De belangrijkheid der constitutie on der oogpunt van kanker en

tuberculose). Torfs (A.), Vlaamsch. geneesk. Tijdschr. (Gent), 1922, 3, 581-588.

Constitution, which is conditioned by endocrine and sympathetic factors, is important in relation to cancer and tuberculosis.
—J. K.

Functional tests in ENDOCRINOLOGY. Ulrich (H. L.) & Rypins (H.), J. Lancet (Minneap.), 1921, 11, 364-370.

A comment on the value of functional tests in general and their possible value in endocrinology. They conclude that in the opinion of the majority of workers the estimation of the basal metabolic rate is of permanent value as a clinical function test in endocrinology since it is based on well established physiological facts, that the sugar tolerance test is of questionable value because an adequate method for testing this function has not been developed; and that the adrenalin chloride test is an empirical one and should be abandoned as a functional test since it is not based on any established function.—F. C. P.

An attempted ENDOCRINE explanation of vomiting in pregnancy (Versuch einer Erklärung des Wesens des Schwangerschaftserbrechens). von David (M.), Zentralbl. f. Gynak. (Leipz.), 1922, 46, 1067-1069.

The disorder is due to foreign (male) protein —J. K.

(ENDOCRINE) Experimental studies on the value of organotherapy (Experimentelle Untersuchungen über den Wert der Organotherapie). Zondek (B.), Arch. f. Gynak. (Berl.), 1922, 117, 19-26.

General discussion of the utility of incretory materials according to the method of preparation. It is concluded that transplantation or the use of chemically unaltered dried glands is the best and that organ extracts are not specific.—F. S. H.

(GONADS) Morphological significance of the endocrine tissue of the TESTICLE of Urodeles (Signification morphologique du tissu glandulaire endocrinien du testicule des Urodèles). Aron (M.), Compt. rend. Acad. d. sc. (Par.), 1922, 174, 332-335.

(GONADS) The determination of the sexual characters in the Urodeles (Sur le déterminisme des caractères sexuels chez les Urodèles). Aron (M.); Compt. rend. Acad. d. sc. (Par.), 1922, 174, 709-712.

The interstitial cells of the GONADS of cattle with especial reference to their embryonic development and significance. Bascom (K. F.), Am. J. Anat. (Phila.), 1923, 31, 223-259.

A histological study has been made of the gonads of cattle from the early fetal to the adult stage. Evidence has been secured

(GONADS) The influence of pregnancy on vascular tonus (*Der Einfluss der Schwangerschaft auf den Gefäßtonus*). Hinselmann, Arch. f. Gynäk. (Berl.), 1922, 117, 161-171.

Increased tonus of pregnancy may be due to placenta toxins, or optone or more probably to heightened activity of the adrenals or hypophysis, when it is not of pathological origin.—F. S. H.

(GONADS) The influence of specific hormones on OVARIAN activity (*Beeinflussung der Tätigkeit der Ovarien durch innesspezifische Hormone*). Kuhn, Monatschr. f. Geburtsch u. Gynäk. (Berl.), 1922, 49, 128-135.

A comparative study of luteoglandol and ovoglandol showed the former to be more efficacious. Several brief case reports are made of patients with disturbed menstruation.—F. S. H.

The significance of the female GONADS in renal DIABETES (*Die Bedeutung der Funktionen der weiblichen Genitalorgane für die renalin Diabetes*). Küstner (H.), Arch. f. Gynäk. (Berl.), 1922, 117, 158-161.

Clinical observation and experiments on animals lead Küstner to the conclusion that the glucosuria during pregnancy and menstruation, and the lowered sugar tolerance during menstruation is a result of a change of ovarian activity.—F. S. H.

(GONADS) The protective tissue of the interstitial gland of the TESTICLE in the boar (*La tissue de soutien de la glande interstitielle due testicule chez le sanglier et chez le verrat*). Lacoste (A.), J. de méd. de Bordeaux, 1921, 51, 356.

The interstitial tissue of the testis of these animals is highly developed.—F. S. H.

(GONADS) Organ and radiation therapy in the genital hypofunction and hypoplasia of the female (*Organ und Strahlentherapie in ihren Einfluss auf die genitalen Hypofunktionen und Hypoplasien des Weibes*). Landecker (A.), Arch. f. Gynäk. (Berl.), 1922, 117, 376-383.

(GONADS) Supplementary note on twins in cattle. Lillie (F. R.), Biol. Bull. (Woods Hole), 1923, 44, 47-78.

Additional cases of freemartins are described and the author restates his theory that the freemartin represents a zygotically female individual modified by the hormones from the blood of a male twin. The hormones are transferred from one twin to the other by anastomosis of the fetal circulations. It is pointed out that the interstitial cells of the testis develop early in fetal life, while it is doubtful whether the ovary produces a hormone till after birth. The case is different, therefore, from that of transplantation of gonads in mammals. In the freemartin the testicular hormone acts

before the development of an ovarian hormone and inhibits the growth of the ovary. The limitations of the theory are pointed out. It should not be applied to all cases of hermaphroditism in cattle, nor should it be extended without further investigation to intersexuality in other mammals.—M. M. H.

(GONADS) Further experimental investigations on the hypertrophy of the sexual glands. Lipschütz (A.), Wagner (C.), Tamm (R.) & Bormann (E.), *Proc. Roy. Soc. B.*, 94, 1922, 83-92.

A report of the results of an experimental study of varying degrees of castration in a series of guinea pigs. These authors found that after the removal of one testicle or one ovary in young animals the remaining gland hypertrophied and in some instances became twice the size of the normal gland, that small ovarian fragments remaining in the body after removal of one whole ovary and part of the second hypertrophied and attained the weight of an entire ovary, that testicular fragments remaining in the body after the removal of one whole testicle and part of the second did not hypertrophy, this lack of hypertrophy not being due to the degeneration of the seminiferous tubules. Since very small testicular fragments are sufficient for the development of those sex characters which depend upon the internal secretion of the testicle, it follows that the hypertrophy of the seminiferous part of the testicle after unilateral castration is not a compensatory one. The difference between the behavior of an ovarian and testicular fragment seems to be due to the fact that in the ovary the primordial follicles represent a source of hypertrophy, while in the testicle the single tubules can attain only the same climax as those in the normal testicle.—F. C. P.

(GONADS) OVARY and libido (Eierstock und Geschlechtstrieb). Mansfeld (O. P.), *Arch. f. Gynäk. (Berl.)*, 1922, 117, 294-298.

(GONADS) Atrophy of the TESTICLES from nervous lesions (Atrophie testiculaire par lésions nerveuses). Marconi (P.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 356-358.—T. C. B.

(GONADS) The relation of anomalies of follicle and CORPUS LUTEUM formation to uterine anomalies (Die Anomalien der Follikel-und Corpus-luteum-Bildung in Zusammenhang mit den Uterus anomalien). Meyer (R.), *Ztschr. f. Geburtsch. u. Gynäk. (Stutt.)*, 1920, 83, 842-843.

(GONADS) The so-called CORPUS LUTEUM persists in the light of hidden pregnancy [Die sogenannte Corpus-luteum-Persistenz in Lichte einer verborgenen oder Scheinschwangerschaft (okkulte oder Similigravidität)]. Meyer (R.), *Ztschr. f. Geburtsch. u. Gynäk. (Stutt.)*, 1920, 83, 843-844.

Speculation.—F. S. H.

(GONADS) The lipoids of the human OVARY (Ueber die Lipoiden im menschlichen Ovarium). v. Mikulicz-Radecki (F.), Arch. f. Gynäk. (Berl.), 1922, 116, 203-251.

Human ovaries from the 3d fetal month to the climacteric were analyzed for their fat content. The details of the results are too extensive for concise abstracting. Marked differences in amount and distribution of the various general types of lipoids were found. A good review is given.—F. S. H.

(GONADS) A case of infantilism. Miura (H.) & Numata (S.), Tokyo Iji-Shinshi, 1922, No. 2287, No. 2288 (July); cit., Jap. Med. World (Tokyo), 1922, 2, 324.

(GONADS) Primary OVARIAN exophthalmos. Nishioka (M.), Chugwai Iji-Shimpo, 1922, No. 1016 (July); abst., Jap. Med. World (Tokyo), 1922, 2, 326.

The author reports a case of exophthalmos, which was completely and rapidly cured by the extirpation of a diseased ovary in a woman of 25 years. He concludes that the ovarian affection caused the development of exophthalmos.—R. G. H.

(GONADS) TESTIS opotherapeutics. Pavlov (M. M.) & Popov (N. W.), Vrach. Delo, 1919, No. 17, 570-579.

Under the influence of a protein-free extract of the testis the blood pressure temporarily falls, the pulse pressure increases, and a slowing of the heart is observed. The authors suggest that testicular extracts oxidise adrenaline in the blood and thus moderate its action on the vascular system.—Physiol. Abst., 7, 615.

(GONADS) Interstitial tissue and secondary sex characters in birds. Response to J. Benoit (Tissu interstitiel et caractères sexuels secondaires des oiseaux. Réponse à J. Benoit). Pézard (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 245-247.—T. C. B.

(GONADS) Criticism of the theory of Bouin and Ancel (Critique de la théorie de Bouin et Ancel). Pézard (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 333-335.—T. C. B.

(GONADS) Action of the PLACENTA optone (Wirkung der Placentaoptone). Puppel (E.), Arch. f. Gynäk. (Berl.), 1922, 116, 577.

Rabbits were used in these experiments. They were injected with placenta extracts and for comparison with thyroid and ovarian extracts. The placenta extract alone caused uterine enlargement which is considered as an active growth and not an edematous or inflammatory response. The result is considered as evidence for the specificity of the hormone.—F. S. H.

(GONADS) Structure of the TESTICLE of the chimpanzee and the physiological results of grafting (Structure des testicules d'un

chimpanzé et résultats physiologique de leur greffe). Retterer (E.) & Voronoff (S.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 339-340.—T. C. B.

(GONADS) Feeding experiments on tadpoles: PROSTATE gland and other substances. Rogoff (J. M.) & Rosenberg (W.), *J. Pharmacol. & Exper. Therap. (Balt.)*, 1922, 10, 353-358.

Tadpoles were fed human prostate and commercial preparations of ram's and bullock's prostate. Fresh liver, boiled liver, lymph glands, cattle blood serum, cracker dust and brewer's yeast were used as control feeding substances. The authors conclude that a number of substances may increase growth or hasten slightly metamorphosis, but there is no evidence that any of these substances including prostate has a specific effect comparable to that caused by thyroid feeding.—G. E. B.

(GONADS) Nervous symptoms of endocrine origin in women and treatment with ovobrol (*Nervöse Erscheinungen auf innersekretorischer Basis bei der Frau und deren Behandlung mit Ovobrol*). Runze, *Fortschr. d. Med. (Berl.)*, 1922, 40, 665-667.—J. K.

(GONADS) Unilateral gynecomastia (*Eenisidig gynækomasti*). Sand (K.), *Festskr. til Thorkild Røvsing (Copenhagen)*, 1922, April 26, 8pp.

The author discusses the relations between the physiology of the mamma and the sexual glands. He reports the case of a young man of 21 years who desired amputation of the right mamma, which was often tender upon pressure and which handicapped him as a sportsman. The left mamma was normal; the right mamma presented a virginal aspect. Otherwise he appeared absolutely virile—the genital organs were normal and his sexual life was natural. The right mammary gland was subcutaneously amputated. Microscopic examination showed connective tissue with few cells, containing dispersed acini; here and there they were somewhat dilated, but in other respects the construction was like that of virginal mammal tissue. No signs of tumor were apparent.—K. H. K.

(GONADS) Hermaphroditismus (verus) glandularis alternans in a child of 10 years. Sand (K.), *Ugesk. f. Læger (Copenhagen)*, 1922, 84, 921-933.

The case is described of a "boy" of 10 years whose parents are uncertain concerning his sex. His aspect is predominatingly masculine, although he has weak and fine features. He presents labia majora, very small labia minora, a vulva and a very hypertrophic clitoris, 5 cm. long. The orifice of the urethra is slightly behind the clitoris. Psychically he presents both boy-like and maiden-like features; he is very intelligent. Exploratory laparotomy presented a small uterus and fallopian tube with fimbriae at each side. At

the right side there was a testis-shaped body, at the left side a somewhat larger ovary-shaped body. Small pieces of each of the glands were removed. Microscopical examination of the first showed the picture of a testis of fetal structure; the other showed a very complicated picture similar to an abnormally differentiated ovary from an early fetal stage. The case belongs to the very rare class of true glandular hermaphroditism. The author considers the difficulties in therapy and discusses its significance from the endocrine point of view.—K. H. K.

(GONADS) Action of the CORPUS LUTEUM on the genital organs (L'appareil lutéinien de l'ovaire. Son action sur les organes génitaux). Schil, Paris méd., 1923, 13, 138-141.

A general review without bibliography.—R. G. H.

(GONADS) Psuedohermaphroditismus internus masculinus. See-dorff (M.), Hosp.-Tid. (Copenhagen), 1921, 64, Dansk kir. Selsk. Forhandl., 90.

A man, aged 24 years, virile of aspect, was operated upon for bilateral inguinal hernia. At the right side there was a large retained testis, epididymus, etc. At the left side there was a normal looking large testis in the bottom of the scrotum, with vas deferens and funiculus; in addition, in this half of the scrotum was a uterus as big as a thumb, with a wide cavity and with a stalk-like structure which entered into the pelvis. Microscopically, it presented a normal uterine structure with typical glandular elements. The sexual life of the patient had never presented any abnormality.

—K. H. K.

(GONADS) Quantitative variations of the glandular and non-glandular interstitial tissue of the TESTICLE of birds with a periodic sexual activity (Sur les variations quantitatives des tissus interstitiels glandulaire et non glandulaire dans le testicule des oiseaux à activité sexuelle périodique). Benoit (J.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 205-207.—T. C. B.

(GONADS) A case of EUNUCHOIDISM. Sumiwo (S.), Chugwai Iji-Shimpo, 1922, No. 1013; cit., Jap. Med. World (Tokyo), 1922, 2, 325.

(GONADS) Concerning Steinach's F-cells (Zur Frage von Steinach's F-Zellen). Scheunig (F.), Arch. f. Gynäk. (Berl.), 1922, 116, 660-683.

Discussion and histological study of human testes in embryonic and fetal stages. It is concluded that the male puberty-gland cells are of germinal epithelial origin; they are "genitaloid" cells. They reach their maximum development at the end of the fourth fetal month and decrease with the sudden increase in the germ elements

in the fifth month. Whether the interstitial cells are incresory cells is not determined.—F. S. H.

(GONADS) Malignant tumors of the TESTIS. Schultz (O. T.), Chicago Path. Soc., 1921, 11, 185-195.

Schultz made a study of 15 malignant tumors of the testis sent to the pathological laboratory of Michael Reese Hospital. He concludes that sarcoma of the human testis is rare. The few undoubted spindle cell sarcomas which have been reported appear to have arisen in the tunics of the testis or epididymus. The vast majority of malignant tumors of the testis are epithelial. These tumors fall into two main groups. In one the atypical tissue is solid, medullary and composed of closely packed large polyhedral cells. To this type the term sarcoma is frequently misapplied. The large cell medullary tumor is derived from the germinal epithelium of the seminiferous tubules. For this the name spermatocytoma is suggested. In the second group the atypical tissue has a glandular or papillary character. Most tumors of this group contain heterologous tissues. All are probably teratomatous in origin. For this kind of tumor Ewing's designation of embryonal carcinoma may be retained. The embryonal carcinoma may be further subdivided according to the origin of the proliferating epithelial elements: hypoblastic (characteristically adenocarcinomatous; trophoblastic (chorioma); epiblastic (solid, nonglandular alveoli of basal cell type, or rosettes of neuroepithelial origin).—J. P. S.

(GONADS) The pathogenesis of meno- and metro-rrhagia (Beiträge zur Pathogenese der Meno- und Metrorrhagien). Seitz (A.), Arch. f. Gynäk. (Berl.), 1922, 116, 252-290.

A good review in which endocrine factors of ovarian origin are included.—F. S. H.

(GONADS) The use and abuse of CORPUS LUTEUM extract in the toxic vomiting of early pregnancy. Taylor (J. S.) & Taylor (S. P.). Penn. M. J. (Harrisburg), 1923, 26, 252-255.

A few speculations regarding the function of the corpus luteum are offered and arguments for and against the use of this substance in the toxic vomiting of pregnancy are advanced. Of little endocrine interest.—I. B.

(GONADS) The use of small doses of x-rays in amenorrhea and other cases of hypo-ovarianism (Über die Anwendung kleiner Röntgendosen bei Amenorrhoe und anderen auf Unterfunktion der Ovarien beruhenden Anomalien). Thaler (H.), Klin. Wchnschr. (Berl.), 1922, 1, 2454.

No details are given.—J. K.

(GONADS) Case of virginal menorrhagia (*Un case rebelle de ménorrhagie virginale*). Van der Elst (M.), *Gynéc. et Obst. (Par.)*, 1922, 6, 434-436.

A patient of 19 was troubled with constant uterine hemorrhage resulting in anemia, vertigo, dyspnea, constipation, vomiting, and lack of appetite. Cardiac, renal or hepatic etiology were not sustainable. The slight retroflexion of the uterus, or a possible ovarian sclerosis were not obvious causative factors. Treatment with pitréanaline followed by ovarian opotherapy gave relief.

—F. S. H.

(GONADS) TESTICULAR grafts (*Injertos testiculares*). Voronoff (S.), *Arch. de med., cirug. y espec. (Madrid)*, 1922, 9, 97-106.

Voronoff reviews his work during the past 4 years on gonad transplantation. He believes that the incision that the transplanted testicle adds to the blood stream stimulates the activity of all organs. He claims that the infirmities of old age, both physical and mental, can be combatted by gonad transplantation. Whether we shall be able by means of the same medium to prolong life, Voronoff believes that our experiences are of too recent date to determine with respect to man, but states that the life of animals has been prolonged in this way, citing as an instance rams that have lived 3 or 4 years longer than their usual maximal age after having been subjected to this operation.—W. H.

(GONADS) The influence of the internal secretions on the development of the secondary sex characteristics (*Der Einfluss der inneren Sekretion auf die Ausbildung der sekundären Geschlechtsmerkmale*). Weil (A.), *Arch. f. Frauenk. u. Eugenik. (Leipz.)*, 1922, 8, 118-126.

A brief review of some of the important literature leads the author to the conclusion that secondary sexual differentiation can be explained by assuming differential degrees of incretory gland activity.—R. G. H.

(GONADS) Body structure and psychosexualism (*Körperbau und psychosexueller Charakter*). Weil (A.), *Fortschr. d. Med. (Bérl.)*, 1922, 40, No. 22-23 (June).

Ten subjects of psychosexual infantilism showed a fairly symmetrical decrease in the standard skeletal measurements. Four homosexual males were somewhat long legged and in pelvic and shoulder measurements approached the feminine type. Ten women of the virile type tended toward masculine pelvic and shoulder measurements.—R. G. H.

(GONADS) Comparative microchemical researches on the content of the interstitial and of the lutein cells in the OVARY of the rabbit (*Ricerche comparative di microchimica sul contenuto delle cellule*

midollari e luteiniche dell' ovale di coniglia). Zalla (M.), Arch. ital. di anat. e di embriol. (Firenze), 1921, 18, 475-484.

Four rabbits were studied, two pregnant, one killed immediately after delivery and one 40 days after delivery, the findings being essentially the same in all. For numerous tinctorial reactions the original may be consulted.—G. V.

Evolution of the hormone of the infundibulum of the PITUITARY gland in terms of histamine, with experiments on the action of repeated injections of the hormone on blood pressure. Abel (J. J.) & Rouiller (C. A.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, 20, 65-84.

A method is described for obtaining from the posterior lobe of the hypophysis a pressor-oxytocic principle which is equal in oxytocic activity to from 12 to 18 times its weight of histamine hydrochloride. The first intravenous injection is followed by a pure pressor effect, while a later injection gives a distinct fall in blood pressure. The secretion of urine in the rabbit is reduced or inhibited altogether by a small intravenous injection. It is believed that the vasomotor, oxytocic and renal actions are all effected by a single hormone in the preparation.—G. E. B.

Action of HYPOPHYSEAL extract (Experimentelle Untersuchungen über die Wirkungsweise der Hypophysen extrakte). Anderes, Arch. f. Gynäk. (Berl.), 1922, 117, 299-301; see also, Klin. Wchnschr. (Berl.), 1922, 1, 1760.

Inconclusive results.—F. S. H.

Influence of extract of HYPOPHYSIS on the imbibition of tissues. (Influence de l'extrait d'hypophyse sur l'imbibition des tissus). Biasoti (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 361-362.—T. C. B.

(HYPOPHYSIS) Sisters with dystrophia adiposogenitalis (Geschwisterpaar mit adiposo-genitaler Dystrophie). Biedl, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1630.

Demonstration of two patients and a photograph of a third case. In these cases not the slightest symptoms suggesting hypophyseal disorders existed. The author believes, however, that there exists a cerebral adiposity, with an important metabolic center located in the interbrain, and that cerebral as well as hypophyseal cases of Fröhlich's syndrome probably occur. The same is true of diabetes insipidus.—J. K.

Common PITUITARY syndromes. Blumgarten (A. S.), Med. Clin. N. Am. (Phila.), 1922, 6, 687-718.

In this paper are included reports of 2 cases of pituitary tumor and 4 cases of functional pituitary syndrome characterized by

abdominal manifestations. The symptoms of pituitary tumor are referable to (1) intrasellar pressure, especially headache, vomiting, and eye symptoms; and (2) disturbances of genital function, of bony growth, of carbohydrate metabolism, and of salt and water metabolism. Functional pituitary syndromes are due to physiological or pathological hypertrophy of the pituitary, giving rise to intrasellar pressure plus abdominal cramps which may resemble the symptomatology of such abdominal lesions as gastric ulcer, gall bladder disease, appendicitis, ureteral affections, and the like. Attacks of colic are always preceded by characteristic supra-orbital and bitemporal headache, which is frequently associated with blurring of vision and dizziness. Treatment of the syndrome consists in the administration of pituitary extract, supplemented if necessary by antispasmodics, corpus luteum, and a protein-free diet.—I. B.

Uterus rupture after one injection of HYPOPHYSIS extract (*Rupture de l'utérus après une injection d'extrait hypophysaire*). Sejournet & Braine, *Gynéc. (Par.)*, 1922, 24, 618.

The effect of HYPOPHYSEAL extracts upon the water metabolism of the frog (*Beitrag zur Kenntnis der Wirkung von Hypophysen-extrakten auf den Wasserhaushalt des Frosches*). Brunn (F.), *Ztschr. f. d. ges. exper. Med. (Berl.)*, 1921, 25, 170-175.

Pituitrin does not affect the intact frog's urine secretion, although perfusion of the isolated frog kidney with a pituitrin solution causes contraction of the glomerular vessels. Pituitrin has a specific effect only upon extrarenal water metabolism. Frogs kept in water without nourishment do not appreciably vary in weight. After subcutaneous or intravenous injection of 1 cc. pituitary extract (various preparations were used) weight increased on an average of 12%, with the maximum after 8 to 12 hours and a return to normal usually in 24 to 36 hours, but in some cases 3 to 4 days. Extirpation of frog kidneys showed that the weight increase did not depend upon hindrance of urine secretion. The weight of nephrectomized frogs increased at first about 2 gm. daily, and gradually increased. The frogs usually died on the fifth day from extensive edema. Injection of pituitrin on the day following the operation caused sudden increase of body weight. Exsiccation of frogs in wire cages was not retarded by pituitrin, nor did exsiccated frogs if brought into water reach normal weight more quickly. The pituitrin-water-retention in the frog differs from that of man only in extrarenal factors.—A. B.

Reports on biological standards. I. PITUITARY extracts. Burn (J. H.) & Dale (H. H.), *Med. Res. Coun., Spec. Rep. Ser.*, 1922, No. 69.

Using the isolated uterus of the virgin guinea pig as a test for making quantitative estimations of pituitary extracts, it is found

that the only suitable standard for comparison is a preparation of the pituitary extract itself. Chemical substances such as histamine or KCl are of no use, because the sensitiveness of different uteri varies differently towards a pituitary extract on the one hand from the variation to histamine or KCl. It is shown that, unlike the suprarenal gland, in which the amount of active principle varies in different animals, the pituitary glands of oxen contain approximately the same amount of activity per gm. of material, even though the glands are obtained at different seasons of the year. Consequently, provided the process of obtaining and extracting the glands is kept constant in all details, an extract of fresh glands may serve as a standard of reference for commercial extracts made by large scale methods. A considerable part of the variation observed in commercial extracts at present on the market is due to the fact that different manufacturers make extracts of different strengths. It is recommended that all extracts should be 10%.—Physiol. Abstr., 7, 612.

Tumors of the HYPOPHYSIS. Cohoe (B. A.), Penn. M. J. (Harrisburg), 1923, 26, 328-330.

A brief description of the symptomatology of pituitary tumor, and the report of a case. The patient was a married woman of 59 in whom an adenoma of the pituitary progressed to the stage of rupture on the floor of the sella and invasion of the sphenoidal cells. The local pressure effects of the mass on neighborhood structures were so striking as to render inconspicuous the signs of any functional involvement of the gland. Operation was performed by Dr. Cushing. One month later, following a brief improvement in vision, the sight again began to fail. A course of radium treatment yielded no improvement. The administration of pituitary extract was likewise a failure. Subsequently, however, though the vision was about the same, the general condition of the patient was good, and there were no evidences of pituitary hypofunction.—I. B.

Concerning some of the ocular interpretations of disorders of the PITUITARY body and their non-surgical treatment. deSchweinitz (G. E.), Virginia M. Month. (Richmond), 1921, 48, 179-183.

A discussion of the ocular manifestations commonly present in pituitary body disorders, and suggestions in medicinal treatment. Impairment of vision may vary from a mere blurring of sight to complete blindness, according to the degree of disturbed function of the optic pathways. This, in turn, depends upon the degree of compression of the chiasm, tracts, and optic nerves, but does not bear any close relation to the size of the sella. For instance, in acromegaly, the size of the sella may be conspicuous, but the vision is good. Other eye phenomena associated with pituitary disorders are lesions of the optic nerve, alterations of the visual field, and anomalies of ocular motility. In general, deSchweinitz has had

with an induced current produced polyuria. However, as an electric current may be transmitted over a considerable distance, it cannot be said that this trauma was limited to the gland itself, or that the urinary increase was of hypophyseal origin. By traction on the stalk with effort to avoid trauma to the gland itself, Hanchett states that he was able to produce polyuria regularly. He was able also to regulate the degree of this increase, moderate or extreme, by modifying the amount of traction exerted. Other animals operated upon, in which the same procedure was followed except for traction on the stalk, showed no or only slight polyuria. The 3 outstanding experiments to which the author calls special attention were those on dogs 2, 15 and 55. In dog 2, the opening in the sphenoid bone was made so far posterior that the hypophysis was not exposed, and the stimulation (cauterization) was applied to the region of the corpora mamillaria. In dog 15, due to peculiar anatomic arrangements, the gland came through the dural incision with considerable force, followed by a larger amount of cerebrospinal fluid than had usually been observed. Except for these variations nothing was done which had on previous occasions produced more than a negligible increase in urinary secretion. In dog 55 there was found at postmortem examination a hemorrhage into the third ventricle. The associated polyuria was most marked in this group. Hanchett concludes that "polyuria associated with pituitary disease is, to borrow an expressive phrase, a 'neighborhood symptom'."—J. P. S.

Normal diuresis and diuresis due to HYPOPHYSECTOMY (*La diuresis normal y provocado de los perros sin hipofisis*). Houssay (B. A.) & Hug (E.), *Rev. Asoc. med. argent.* (Buenos Aires), 1921, 34, Sec. Biol., 56-61.

Hypophysectomized dogs usually have urinary output normal in quantity and quality, though in the first few days transitory polyuria is sometimes seen. Water administered by mouth is eliminated more slowly in these dogs,—46% in 3 hours instead of 60%, the rate in the controls.—B. A. H.

Polyuria by extirpation of the HYPOPHYSIS in dogs with degenerated kidneys (*Polyurie par extirpation de l'hypophyse chez des chiens à reins éternés*). Houssay (B. A.) & Rubio (H.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 358-359.—T. C. B.

Disease of the HYPOPHYSIS (*Hypophysenerkrankung*). Jungmann, *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1628.

The disease began with symptoms of diabetes insipidus (thirst, polyuria). Later, these symptoms became much less intense and only an increased NaCl production and general hyperosmosis of the blood remained. At postmortem examination, purulent appendicitis and an abscess of the hypophysis were detected. The author explains the improvement of the diabetes insipidus by stating that

pressure of the abscess on the interbrain was lessened as the symptoms of the inflammation became less intense.—J. K.

Blindness of PITUITARY origin and organotherapy. Kern (M.), *Am. J. Clin. M. (Chicago)*, 1923, 30, 18-22 (January).

Detailed case report with theoretical discussion. The "organotherapy" (nature not specified) resulted in spectacular restoration of vision.—R. G. H.

(HYPOPHYSIS) The practical importance of some obstetrical methods (*Over die practische waarde van eenige obstetrische handelingen*). Koek (C.), *Inaug. Dissertation*, Leiden, 1922.

Dutch opinion differs as to the value of pituitrin. Kouwer, professor of obstetrics at the University of Utrecht, opposes its use (see *Endocrin.*, 1922, 6, 156, 314). Koek sent questionnaires to all Dutch doctors who practice obstetrics. Eighty per cent of these doctors used pituitrin; 7% were not satisfied. Most of these complained of the inactivity of the drug. This is probably because the Dutch preparation (pituitrin-Blomberg) is often inactive. Some complained that pituitrin would sometimes cause spasms of the ostium uterinae, and difficulty in removing the placenta. Some thought that pituitrin endangered the life of the child, and that it would sometimes produce collapse in the mother, especially during the first hour after birth. Most of the physicians reported that pituitrin lessens the time of labor and decreases the use of forceps.—J. K.

(HYPOPHYSIS) Diagnosis of the lesser hypophyseal syndromes (*Diagnostic des petits syndromes hypophysaires*). Léopold-Lévi (M.), *Médecine (Par.)*, 1923, 4, 342-348.

Léopold Lévi divides the syndromes of the hypophysis into hypopituitarism, hyperpituitarism, and instability of the hypophysis. He analyzes their morphologic, nervous, visceral, and metabolic symptoms in the different stages of the evolution, expressing his ideas in detailed tables of symptoms.—R. G. H.

PITUITRIN in obstetrics. Mendenhall (A. M.), *Indianapolis M. J.*, 1921, 24, 191-196.

Mendenhall calls attention to the many dangers in using pituitrin in obstetrics and advises its use only in selected and carefully supervised cases.—F. C. P.

(HYPOPHYSIS) A case of acromegaly. Okabe (Y.), *Fukuoka Ikadaigaku Zasshi*, 1922, 15, No. 4 (July); *cit.*, *Jap. Med. World (Tokyo)*, 1922, 2, 329.

HYPOPHYSIS and pregnancy (*Hipófisis y gestación*). Perez (M. L.), *Semana méd. (Buenos Aires)*, 1921, 28, 540-548; 580.

General description of the anatomy, embryology, histology and physiology of the hypophysis. The author observed 10 pregnant, 9 nonpregnant and 4 male, hypophysectomized dogs. All of the pregnant females died within 24 hours. Mortality in the other animals was about 60%.—B. A. H.

The basal metabolism in **HYPOPHYSEAL** diseases (Ueber den respiratorischen Gasswechsel bei Erkrankungen der Hypophysis). Plaut (R.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1413.

See Endocrin., 6, 715.—J. K.

A case of meningeal endothelioma simulating a tumor of the **HYPOPHYSIS**. Portis (B.), Tr. Chicago Path. Soc., 1922, 11, 303-306.

Report of a case of a woman aged 50 with autopsy findings of an endothelioma of the meninges extending over the hypophysis with pressure enlargement of the sella turcica. The woman was very obese.—J. P. S.

Some lesions of the **HYPOPHYSIS**. Simonds (J. P.), Tr. Chicago Path. Soc., 1921, 11, 183-185.

A small abscess in the posterior hypophyseal lobe was reported from a patient with multiple septic infarcts, also a condition in which the cells from the middle lobe grow backward into the neurohypophysis. This condition is relatively common in old age. Islands of abnormal cells in the posterior lobe were also described. These cells are unlike any of the cells of the anterior or middle lobes, and are not connected, as shown by serial sections, with the backward growth of cells from the middle lobe. Their significance is unknown. Hemangioma-like structures were found in the anterior lobe. These appear to be quite constant and can be readily demonstrated by serial sections. Small masses of lymphoid cells were occasionally found along the line of junction between the middle and posterior lobes. Their significance is not known. Congenital syphilis of the hypophysis, the characteristic feature, is a rather uniform increase of connective tissue between the cords of cells in the anterior lobe. An adenoma of the hypophysis was also reported from a patient with no acromegaly or other disorder of the hypophysis.—Author's Abst.

Action of extracts of **HYPOPHYSIS** on bulbar polyuria (Action des extraits d'hypophysis sur la polyuria bulbaire). Solari (L. A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 359-360.

Case of dwarf having **PITUITARY** derangement. Takimoto (S.), Chugwai Iji-Shimpo, 1922, No. 1013, 1014; cit., Jap. Med. World (Tokyo), 1922, 2, 325.

The influence of **PARATHYROID** and **THYROID** tissue on the creatinine-creatinine balance in incubated extracts of muscle of the albino rat. Hammett (F. S.), J. Biol. Chem. (Balt.), 1921, 48, 143-152.

Evidence is presented which demonstrates that the addition of parathyroid tissue to extracts of muscle tissue tends to retard the formation of creatinine normally taking place during incubation. This occurs in acid neutral or alkaline mixtures. The addition of thyroid tissue to similar extracts has no effect upon the creatinine formation that is demonstrable by the methods used. Since the maximum retardation effect of the parathyroids occurs in solutions buffered to neutrality, while the maximum creatinine formation takes place at the same reaction, the conclusion is justified that this parathyroid effect is an expression of a direct influence of the parathyroids on creatine metabolism.—F. S. H.

(**PARATHYROID**) The influence of **TETANIA** gravidarum on the young (Ueber den Einfluss der Tetania gravidarum auf die Frucht). Niderehe (W.), Arch. f. Gynäk. (Berl.), 1922, 116, 360-382.

The possibility of a parathyroid insufficiency being a contributing factor is briefly mentioned.—F. S. H.

Studies in the physiology of the **PARATHYROID**S. Salvensen (H. A.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1923, 20, 204-210.

After partial thyroidectomy in dogs there was a 30% reduction in the serum calcium. After complete parathyroidectomy in 10 dogs, 6 died of tetany. These showed decreased calcium and increased phosphorus in the serum. After intravenous injections of calcium chloride the calcium injected was excreted within 24 hours, largely into the bowel. Four of the parathyroidectomized animals were kept healthy on a diet containing a liberal supply of milk. The calcium in the milk was the essential factor. The calcium of the blood remained low. There was a relation between the tolerance for glucose and the amount of blood calcium. In convulsions produced in healthy animals by guanidin there is no reduction of serum calcium.—J. C. D.

PARATHYROID therapy in calcium deficiency. Vines (H. W. C.), Dementia Praecox Studies (Chicago), 1922, 3, 69-75 (April).

In chronic ulcerative states in which there is chronic toxemia the author has found uniformly a reduction in the ionic calcium of the serum. This is dependent upon partial parathyroid deficiency. In treating these cases, calcium salts alone give no improvement, but when given with parathyroid, 1/10 grain every other day, marked improvement has resulted. More than 100 cases have been

dealt with. Vines believes that clinical evidence supports MacCallum's theory that toxic substances may arise under conditions of parathyroid insufficiency and form combinations with calcium of blood. A short bibliography is appended.—F. H. A.

Physiology of the PINEAL body. Izawa (Y.), Okayama Igakkwai Zasshi, 1922, No. 390 (July).

The endocrine organs that are affected by pinealecotomy are genital glands, i. e., the testes, the ovary and fallopian tubes, besides combs and the bodily development.—Jap. Med. World, 2, 333.

On the influence of the SPLEEN upon red blood-corpuscles. Bolt (N. A.) & Heeres (P. A.), Biochem. J. (Lond.), 1922, 16, 754-764.

Material from sheep was used. The spleen has the power of diminishing the osmotic resistance of the erythrocytes. These are prepared hereby for hemolysis which partially takes place in the organ itself. Erythrocytes from the vena lienalis that have been washed with an equilibrated salt solution do not show this decreased osmotic resistance. This fact is taken to prove that the point of attack of the hemolytic power of the spleen lies in the removable surface layer of the erythrocytes. The alteration in this layer must consist in a decrease of the proportion cholesterol phosphatide.

—F. S. H.

A new function of the SPLEEN (Ueber eine neue Funktion der Milz). Naswitis (K.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1441.

Blood, hemolyzed by freezing and heating, was intravenously injected into dogs from which the blood had been taken. There resulted an increase of the quantity of blood. This was not true, however, when the same experiment was performed on splenectomized dogs. The author concludes that hemolyzed blood does not stimulate directly the blood preparing organs, but that it stimulates the formation in the spleen of substances acting upon the bone marrow. He believes, therefore, that the spleen is probably the "uniform center" of the bone marrow, regulating its activity by the antecses.—J. K.

hypophysis of sclerema neonatorum and hypertrophy of the THYMUS (Sclerema dei neonati con ipertrofia del timo). Action of ex Grimaldi (A.), Arch. di farmacol. sper. (Roma), 1922, 113-117.

Case of dwarf if eosinophil cells in the same organ were the only lesions found in 2 cases of sclerema neonatorum. Chugwai Iji-Shi (Tokyo), 1922, —Physiol. Abst., 7, 619.

(THYMUS) A study of the shadows in the thorax of the newly-born. De Buys (L. R.) & Samuel (E. C.), *Am. J. Dis. Child.* (Chicago), 1922, 21, 397-404.

This study, based upon the observations in 55 infants, was undertaken with the hope of devising some method by which the abnormal shadows in the thorax of the newly-born could be differentiated from the normal. The conclusions obtained were as follows. The heart shadows vary as to shape, size and position. These variations occur with no relation to the size of the infant. The heart shadows may be grouped in several types according to shape, such as globular, adult, drop, nutmeg, round, unusual and unclassified. Variations in size and position occur in each of these types. There is no constant relation between the heart shadow and the shadow of the thymus. The shadow of the thymus is not necessarily influenced by the position of the heart. The shadow of the thymus varies in its size and position independent of the heart shadow and with no relation to the size of the infant. These variations in the shadows of the heart and thymus can exist without clinical manifestations of disease.—M. B. G.

The incidence of THYMIC enlargement without symptoms in infants and children. Greenthal (R. M.), *Am. J. Dis. Child* (Chicago), 1922, 24, 433-441.

An analysis of 2,000 consecutive cases in infants and children ranging in age from 3 days to 12 years. Thymic enlargement was diagnosed in 90 or 4.5%. Of these 90 patients, 87 gave no history and presented no symptoms of thymic involvement. Enlargement of the thymus was noted in 25.6% of all the patients who had a roentgenogram of the thorax made. The finding of an enlarged thymus gland even though there be no clinical evidences of thymic involvement should not be treated lightly. Greenthal believes that pre-operative x-ray treatment of patients who have enlarged thymus lowers the number of operative deaths. Congenital defects and malformations are frequently found associated with enlargement of the thymus. An enlarged thymus has been frequently found in poorly nourished and marantic children. On the other hand, Greenthal noted that just as frequently has he found no thymic enlargement in well nourished children.—M. B. G.

Two cases of sclerema neonatorum with hypertrophy of the THYMUS (*Duo casi di sclerema dei neonati con ipertrofia del timo*). Grimaldi (A. B.), *Arch. di Farmacol. sper.* (Roma), 1922, 34, 95-107; 113-117.

A postmortem report of two female infants who died immediately after birth. Both presented evident signs of sclerema. In both, the heart, thyroid, surrenals, kidneys and liver appeared normal, while their thymus showed accentuated hypertrophy. The

dulla and thyroid and probably with regard to the liver. The introduction of an extremely slight amount of adrenalin into the blood stream will cause marked acceleration of the denervated heart. The same result is obtained if the afferent nerve to the adrenal gland is stimulated. Simple massage of the thyroid gland produces acceleration of the denervated heart, even when the adrenal gland has been previously removed. Likewise stimulation of the cervical sympathetic nerve will produce the same effect by increasing the output of thyroxin into the blood stream. Cannon points out a curious and interesting fact, that these experiments on the thyroid gland produced striking results (as proved by metabolism tests and electrocardiogram records) when performed on animals in November and December, whereas only minor effects and at times none at all resulted when the same experiments were repeated in March and April. The author explains this discrepancy as probably due to the marked variation of the iodine content of the thyroid gland in various seasons of the year, the high period being in September and October and the low period being in March and April. He points out that these seasonal variations in the activity of the glands of internal secretion are full of possibilities of great clinical interest. For example, in animals there are definite breeding seasons and these breeding season are definitely associated with certain periods of the year. Recent studies carried on in school children have shown that the rate of growth of school children in the fall is four times that which it is in the spring months. This suggests that there is a correlation between the rate of growth and the seasonal iodine content of the thyroid.—H. L.

Some applications of **THYROID** therapy. Cobb (I. G.), Prescriber (Edin.), 1922, 16, 328-333.

In addition to its value in hypothyroidism, thyroid therapy is serviceable in chronic toxemias such as intestinal stasis, in rheumatism, and in such acute infections as typhoid fever. The author advocates the use of thyroid substance in disorders of the pituitary, adrenals and thymus, also in nocturnal enuresis and iridocyclitis. Cobb insists that in all cases the initial dose of thyroid must be small.—F. C. P.

(**THYROID**) Circumscribed scleroderma and exophthalmic goiter (Sclérodermie circonscrite et goitre exophtalmique). v. Dubreuilh, Bull. Soc. franç. de dermat. et syph. (Par.), 1921, 28, 221; abst., Schweiz. med. Wchnschr. (Basel), 1922, 52, 595.

A 53 year old woman suffered for 5 years with Graves' disease. Two years ago she developed on the upper thigh 2 symmetrical oval livid plaques.—R. G. H.

(**THYROID**) Some comments on the probable cause of exophthalmic goiter. Dunn (J.), Arch. Ophth. (N. Y.), 1918, 47, 248-255.

On the basis of the work of Rosenow and Billings on focal infections and a study of 4 cases of exophthalmic goiter showing eye symptoms, Dunn concludes that the main agent at work in causing hyperthyroidism is an infectious one, and that the most common location of the focus of infection is the tonsillar crypts. The author does not offer any explanation of the mechanism by which this operates.—J. P. S.

The **THYROID** factor in diabète gras. Friedman (G. A.) & Gottesman (J.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1923, 20, 213-214.

A brief discussion without new facts.—J. C. D.

(**THYROID**) Goiter operations. Grigg (W. F.), *Virginia M. Month. (Richmond)*, 1921, 48, 158-160.

Advocates the use of local anesthesia in goiter operations.
—J. P. S.

(**THYROID: PARATHYROIDS**) Concerning the formation of creatine from methyl guanidine in muscle. Hammett (F. S.), *J. Biol. Chem. (Balt.)*, 1923, 55, 323.

Extracts of muscle tissue of the rat were incubated with methyl guanidine and the material analyzed for total creatinine. Extracts buffered with phosphate mixtures to acid and alkaline reaction, with and without the addition of sodium acetate, parathyroid tissue and thyroid tissue, were studied. Negative results were obtained throughout. No changes in the total creatinine content were observed. In view of this fact the author is inclined towards Biedl's hypothesis that methyl guanidine (supposedly found in the muscle and urine of parathyroidectomized animals) and creatine (found in the muscle tissue of normal animals) are derived from a common precursor as yet unidentified.—Author's Abst.

The refractive index and water content of the blood serum of **THYROPARATHYROIDECTOMIZED** and **PARATHYROIDECTOMIZED** albino rats. Hammett (F. S.), *J. Biol. Chem. (Balt.)*, 1923, 55, x.

Thyroparathyroidectomy induced an absolute increase in the refractive index and solids of the serum. No changes in the nature or the distribution of the refractive substances other than water were found in male rats. Female rats reacted differently because of more intensive growth inhibitions. Parathyroidectomy did not change the absolute amount of water in the serum or the refractive index. Nevertheless, mathematical analysis shows that the nature or the distribution of the refractive substances was altered.
—Author's Abst.

THYROID therapy in eye disease. Harry (P. A.), *Prescriber (Edinb.)*, 1922, 16, 333-334.

Harry advocates thyroid therapy in certain forms of cyclitis, retinal and choroidal hemorrhage, vitreous opacities, optic atrophy, lesions of the cornea, parenchymatous keratitis keratoconus, corneal dystrophies, and glaucoma (when used with various myotics). He reports that myopes do not react favorably to thyroid therapy, and that thyroid amblyopia and exophthalmos may result from the injudicious use of thyroid substance.—F. C. P.

(THYROID) Hypoglycemia in exophthalmic goiter. Holman (E. F.), Johns Hopkins Hosp. Bull. (Balt.), 1923, 34, 69-70.

Twenty-four hours after a double subtotal thyroidectomy in an exophthalmic goiter patient of 17, a condition of semi-stupor appeared. Blood sugar was found to be reduced to 48 mg. per 100 cc. Intravenous glucose relieved the condition. Further studies along this line are recommended by the author as promising valuable data.—R. G. H.

(THYROID) Endemic goiter, cretinism and their prevention (*Über endemische Struma, Kretinismus und ihre Prophylaxe*). Hotz (G.), Klin. Wchnschr. (Berl.), 1922, 1, 2073-2077.

A general review. The author believes that large doses of iodine are a better preventative against goitre than small doses.
—J. K.

(THYROID) Basal metabolism and blood sugar tolerance. Hoxie (G. H.), J. Lab. & Clin. M. (St. Louis), 1922, 8, 112-121.

Report of a study of the relation between the basal metabolism of thyroid activity and carbohydrate tolerance. Deductions are based upon 106 tests on 95 patients. The basal metabolic rate was tested on the closed circuit type of apparatus, namely, the Sanborn Benedict and the Sanborn Handy. The amount of glucose used was 1.75 grams per kilogram of body weight according to the suggestions of Janney. The author derived the following conclusions: the simple closed circuit type of calorimeter is worth while in actual practice; variations in reports on the basal metabolism rate seem due more to the condition of the patient than to the type of apparatus; it is necessary to correlate clinical observation with the laboratory tests; the blood sugar tolerance test cannot be substituted for the calorimeter, nor can any close parallelism be drawn; both studies are needed if a complete knowledge of the patient's function and vitality is sought; a revision of terminology and standards of blood sugar curves is needed if we are to introduce this study into general practice.—I. B.

THYROID and anaphylaxis (*Thyroïde et anaphylaxie*). Houssay (B. A.) & Sordelli (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 354-356.—T. C. B.

The influence of the **THYROID** in some acute infections. Jones (H. S.), *Prescriber* (Edin.), 1922, 16, 317-322.

Since the main function of the thyroid gland is to stimulate metabolism, the activity of the gland is increased in acute infections. The author calls attention to the evidence of hyperthyroidism in acute tuberculosis of the lungs, acute articular rheumatism, diabetes, syphilis, and gonorrhea. He states that the well known effect of pregnancy on acute tuberculosis can best be explained by assuming that prior to pregnancy in a subject suffering with acute phthisis there is a pathological excess of thyroid secretion, that this excess secretion is utilized for physiological purposes during gestation and again becomes pathological after parturition and is manifested by an increased activity of the tubercular lesion. In acute rheumatism the myocardial lesions resemble those of hyperthyroidism. Diabetes is considered as an over activity of the thyroid, adrenal and pituitary associated with hypoactivity of the pancreas. Jones believes that the activity of the thyroid gland is increased in acute syphilis and gonorrhea, basing his conclusions on an army experience in which he noted that the more active the glands, the more virulent the syphilis or gonorrhea. He further calls attention to the increase of leucocytes in hyperthyroidism and points out the effect on disease.—F. C. P.

(**THYROID**) A study of goiter and associated conditions in domestic animals. Kalkus (J. W.), *Bull. State College of Wash. Agricultural Exper. Station* (Pullman), 1920, No. 156, Repr. 48 pp.

From extensive survey work and from experimentation the author reports that hyperplastic goiter is enzootic among all species of domestic animals in certain so-called goitrous regions. It is especially prevalent in certain sections of Washington, Montana and British Columbia. The disease is manifested in somewhat different forms in the different species of domestic animals, but the primary lesion in all cases is of similar character and consists of hyperplasia of the thyroid. This type of goiter is of little importance in the adult, but causes grave disturbances in the newborn. Affected colts, kids, lambs and pigs seldom live, while the condition is less fatal to affected calves. It has not been definitely proved, but it is quite likely that a deficiency of iodine in the water, feed and possibly the soil is responsible for the malady. Other unknown factors may also be considered as causal agents. Feeding experiments indicate that either water, feed or both from a goitrous region may cause goiter. Perfectly controlled experiments with Angora goats show that goiter can be absolutely prevented by administering iodine to does during pregnancy. This can be given either in the form of potassium iodide by mouth or tincture of iodine subcutaneously or on the unbroken skin. Field experiments also indicate that the condition can be successfully prevented in

other species of animals by the use of iodine. A feature of the report is the inclusion of 29 excellent illustrations.—R. G. H.

The THYROID gland and anaphylaxis. Response to R. Applemaus (Glande thyroïde et anaphylaxie. Réponse à R. Applemaus). Kepinow (L.) & Lanzenberg (A.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 165-166.—T. C. B.

(THYROID) Myxedema tarda in constitutional lipomatosis (Spätmyxoedem bei Konstitutioneller Lipomatose). Kisch (F.), *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1644-1646.

Report of the case of a woman of 45 years, 156 cm. in height and about 95 kg. in weight. She had a broad, swollen face; big hands with small, short fingers; and dry skin. Her heart dilated to the right and to the left. The mother had diabetes. Both parents were extremely fat, as was the patient herself. Menstruation was regular but scanty. She had one child. Thyroid treatment had a good effect. The serum contained a very large quantity of proteins; the carbohydrate tolerance was increased; the electrocardiographic findings were typical, as described by Zondek in myxedema (see *Endocrin.*, 1920, 5, 369).—J. K.

(THYROID) Causes, types and treatment of goiter (A contribution to the geographical surgery of the goiter in the Main river country) [Ueber Typen, Ursachen und Behandlung des Kropfes (Ein Beitrag zur geographischen Chirurgie des Maingau-Kropfes)]. Klose (H.), *Med. Klin. (Berl.)*, 1921, 17, 773-775.

Clinical experience has shown that the various forms of goiter correspond with the respective geographical areas within which the several types are found. The author distinguishes 2 types: (1) Highland thyroids with usually considerable degeneration, few blood vessels, and no nerves; the normal parenchyma is diminished to a minimum, thus often causing symptoms of hypothyroidism; (2) low-country thyroids with less degeneration and no hypothyroidism, but often slight hyperthyroidism. Goiters of the Main country (in the vicinity of Frankfurt) are of these two types. The author considers iodine therapy pernicious in these goiters because it causes augmented discharge of colloid.—A. B.

(THYROID) Malignant goiter (Die Struma maligna). Klose (H.) & Hellwig (A.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 1687-1691.

Among 655 goiters operated upon by the author, 20 were malignant (17 women, 3 men). In 18 cases the tumor was a cancer; the other 2 cases were sarcomatous. Trauma seemed to be an important factor in pathogenesis, especially in operations for goiter, and incarceration of substernal tumors had no influence. Nine patients showed metastases in the lungs; 16, in the skeleton. Cachexia was never seen. When the case is properly diagnosed in

the beginning, complete ablation followed by x-ray therapy is the best treatment. When the tumor shows infiltration into the surrounding tissues, however, x-ray treatment alone (exact measuring is important) is preferable.—J. K.

Effects of thyroxin, **THYROID** extract, and sodium iodide, respectively, on neuro-muscular activity in cretin sheep. Liddell (H. S.) & Simpson (S.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, 20, 197-198.

Thyroxin was given to 4 cretin sheep and the spontaneous activity studied. There was a latent period of 3 to 10 days followed by a sharp increase in activity. With sodium iodide there was no increase, while with thyroid extract the increase was not marked by a sharp rise.—J. C. D.

Gastric digestion in **HYPERTHYROIDISM**. Lorenzi (A.), *Gaz. d. osp. e d. clin. (Milan)*, 1922, 43, 660-661; abstr., *Presse méd. (Par.)*, 1922, 30, 1026.

The idea that digestive function is related to the functions of the thyroid goes back to the time of Eppinger. Since then, various and contradictory results have been reported. Lorenzi carried out his experiments with the aid of the x-rays. Some gelatine capsules containing about 0.40 gm. of bismuth were ingested with an experimental meal. The author observed the moment of rupture of the capsules, and thus determined the time of gastric digestion. In the hyperthyroid patients this process seemed to be more rapid than in the normal subjects. This is explained by the fact that the major part of the functions of the stomach are regulated by the vagus which is functionally in relation with the thyroid.—R. G. H.

(**THYROID**) Discussion on the medical and surgical treatment of Graves' disease. Mackenzie (H.) & Berry (J.), *Proc. Roy. Soc. Med. (Lond.)*, 45, Sect. Clin. 1-62.

This lengthy symposium is an important though timeworn debate regarding the respective virtues of surgical, x-ray and medical treatment of Graves' disease, without, in the end, deciding specifically which treatment deserves the medical public's complete confidence. It is only possible, in an abstract, to detail the following salient points of the discussion:

Mackenzie states that though medicinal measures are valuable, there is no specific that the internist might use in Graves' disease. The elimination of infectious foci and a fair trial with medicinal measures result in recovery of many patients, but in some cases surgery or the x-rays must be employed. Thyroidectomy results in marked improvement, and though the eyes still remain prominent, the frightened look usually disappears. Many patients require two or even three operations. Contra-indications to thyroidectomy are:

(1) fear of the operation; (2) mental symptoms; (3) diabetes; (4) auricular fibrillation. X-ray treatment of Graves' disease is successful in many instances, but local scarring, keloid and burns may result from irradiation. The main drawbacks to this treatment consist in the long time required to affect improvement and the difficulty of carrying it out in severe types of the affection.

Barry holds a less sanguine view of the advantages of operation on patients with Graves' disease, because of the tendency to relapse even after the most successful thyroidectomy, and the incompleteness of the cure in many cases that at first sight seem most favorable. Even when performed under the best of conditions, the removal of a hyperplastic goiter involves considerable danger to life—far greater than that of operations for simple goiter. The mortality is at least 3 to 5%, and in many quarters it is far higher. But even a 5% mortality is willingly faced by patients if the operation offers a good chance of cure. The inclusion into surgical statistics of toxic adenoma is misleading. Barry does not approve of operation upon patients who are improving and who do not feel ill, nor does he operate on unwilling patients. He does not approve of "stealing the gland," as he deems it much better to have the patient thoroughly cognizant of what she is to expect. Many patients who have made apparent recovery from the operation and are practically well for a considerable time may relapse or even die of the disease. In some of these a second operation is advisable, but there is a limit to the amount of gland that can be removed, lest the ultimate condition of the patient may be as bad as, or even worse than, the first.

Dunhill states that death is not the only tragedy in Graves' disease. Jessop has collected 25 cases and reported 2 in which an eye had been lost, due to ulceration because of extreme exophthalmos. Operation is not to be entertained until (1) the removal of infectious foci has been effected, (2) the patient has had a period of rest, and (3) symptomatic drug treatment has been given a fair trial. If no improvement occurs after a reasonable time, other measures such as x-ray and operation must be considered. In Dunhill's experience, x-ray treatment is unsatisfactory because it fails to improve the pulse rate, the size of the thyroid, the exophthalmos and the tremors. Again, it produces marked fibrosis in the gland, a process which continues long after the application of the rays, leading to the danger of myxedema. Untreated, some patients recover. Other patients are in various grades of ill health down to the most complete bed-ridden wrecks. Some can do light work, others require considerable rest between activities. Still others, very ill, are possessed of a spirit of restlessness. Again, some are waterlogged from cardiac and renal insufficiency. In still others, an eye is irretrievably damaged. In all of these, improvement under treatment would take years to affect, and in some, improvement is impossible. Most of these patients could be tremendously improved

by operation. Still, Dunhill never operates on a patient with Graves' disease without fear and great anxiety, a feeling which does not leave him until some days after the operation.

Hale-White mentions the case of a woman who was admitted to the ward for operation on exophthalmic goiter. After she had been in a few days, and before the operation, evidence of typical typhoid fever was observed. She was transferred to the medical ward, and under the rest in bed got completely well of her exophthalmic goiter. Hale-White states that the presentation of a few cases recently operated upon is no proof that operation is best, for it is quite as easy to show similar results without operation. At least a hundred patients operated on and followed up for twenty years would have to be shown before definite conclusions as to the efficacy of surgery could be drawn.

Florence Stoney states that she has collected 200 cases of primary Graves' disease and of the syndrome superimposed upon an old bronchocele, all treated by x-rays. Of these, 78 are quite cured and strong up to 12 years after treatment; 1 is slightly myxedematous; 66 are improved and working, though possessing such symptoms as overstrained heart and other manifestations; and 21 are no better. Since treatment, 10 have died. Of the 200 cases, 185 are women and 15 men—the latter cases due to war conditions. The principles of treatment consist in a lessening of the thyroid substances and the removal of the cause. X-ray treatment can accomplish all that surgery can do, with the great advantage that the dose can be graduated so as to destroy the exact amount of tissue desired. Further advantages are the absence of shock of repeated operations, no risk to life and no pain. There are but three disadvantages of x-rays: (1) The improvement is slow, but this could be overcome by an early diagnosis and the early institution of treatment; (2) the possibility of telangiectasis, but an earlier institution of treatment and expertness of application would lessen its occurrence; (3) scarring of the neck; this, too, could be avoided. Stoney urges an early diagnosis when the patient might be "merely run down" with a rapid pulse and a rapid toneless first sound in the heart resembling the second. This is a strong indication of thyroid trouble, and if treated as such would save many patients months of illness. There are other difficulties connected with these patients: (1) the inability to alter the course of their lives; (2) the difficulty of removing mental worry; (3) the presence of exhausting brain work; (4) the presence of old bronchoceles which are liable to break down frequently.

Romanis states that thyroidectomy improves but does not cure the patient. Though there is an increase in weight, a lowering of pulse rate, and an improvement in the heart action, the pulse rate does not reach normal, the heart is still dilated, and the eyes still present exophthalmos. Even multiple operations do not produce

complete cure. In the few cases in which he deliberately removed the entire thyroid gland, the physical signs did not completely disappear. He asks whether the parathyroids are not a physiological myth. Neither he nor other surgeons with whom he has spoken on the subject had ever seen any evidences of tetany arising from operation in which no attention was paid to the parathyroids and in which there had probably been a partial or complete removal of these glands. He is tempted to believe that, in man at least, the parathyroids do not play as important a rôle as the physiologists would have us believe.

Walton states that the surgeon does not see the medical successes because he is not brought in contact with them. He believes the disease is due to thyroid hyperactivity. Surgery is not to be attempted during the first six months of the disease, for medical measures may during this time prove beneficial. He does not believe x-ray treatment to be of much service in the treatment of this disease. He advises medical treatment also as a preliminary to surgical treatment, and in cases in which too little thyroid has been removed by the surgeon.

Hernaman-Johnson emphasized the fact that Graves' disease cannot be produced by thyroid feeding, but that the affection is probably produced through the sympathetic nervous system and all the endocrine organs. Since the precise cause of Graves' disease is unknown, treatment must be symptomatic and empirical. Surgery is symptomatic treatment, as it breaks one of the vicious circles constituting the syndrome. X-ray treatment is administered with the same idea, but roentgen therapy is productive not only of local results but constitutional benefits as well.

Joll states that a careful search of his patients for infectious foci leads him to conclude that there is no ground for believing that Graves' disease is caused by intestinal or any other type of toxemia. Though the diagnosis of the disease is not difficult, yet he sees many patients diagnosed as Graves' disease who are really suffering from encapsulated tumors. Joll advocates early diagnosis and early operation in practically all cases.

Williams states that operations on the thyroid gland are inadmissible in Graves' disease. The disease is not only not a hyperthyroidism, but is not a disease of the thyroid gland at all. Many patients with advanced stages of the affection present no enlargement of the organ. Exophthalmos is due to adrenal excess, and heart symptoms to thymus enlargement. Graves' disease is a toxemia in which all the members of the endocrine family are involved. Treatment consists in the discovery and elimination of the causal toxin, which in the large majority of cases is gastrointestinal in origin. The enlarged thymus is also responsible for many of the nervous symptoms by its pressure upon the pneumogastric, the sympathetic, and the phrenic nerves. The mental

symptoms may also be produced by the enlarged thymus because of interference with the drainage system from the brain. There is no more justification for the removal of a lobe of the thyroid in Graves' disease than there is for the removal of one kidney in diabetes.

Wilson agrees that exophthalmic goiter is not a disease of the thyroid gland; it is a neuro-glandular disease. At present the disease is being treated from without, but he hopes that it will soon be treated from within.

Berry, in closing the discussion, states that many cases prove the efficacy of irradiation. He regards a patient as cured when the nervous symptoms disappear and do not return; he pays no attention to the neck and to the eyes, though in many cases these show improvement.

Mackenzie, in the course of his closing remarks, states that medical treatment must not be underrated. The surgeon is not in position to pass judgment upon the efficacy of medical treatment in Graves' disease.

Throughout the discussion the terms hyperthyroidism and exophthalmic goiter are used interchangeably.—I. B.

(THYROID) Iodine in natural waters in relation to goiter. McClendon (J. F.), *J. Biol. Chem. (Balt.)*, 1923, 55, xvi.

McClendon burns foodstuffs in a bomb-calorimeter to prevent loss of iodine. Foodstuffs derive iodine from soils, and river water represents leachings from soils. In the Mississippi river system, in Minnesota, iodine averages 0.8 per billion and goiter 8 per thousand troops; in Missouri iodine is increased to 2 and goiter reduced to 4. A discussion of chlorine and iodine distribution is given. Rats fed KI show small thyroids.—F. S. H.

The application of results obtained in experiments on the hyperplasia of dogs' THYROIDES to the treatment of exophthalmic goiter (Graves' disease). Mellanby (E.) & Mellanby (May), *Proc. Physiol. Soc. (Lond.)*, 1921-22, 55, p. x.

The authors were impressed with the similarity in histological appearance and in therapeutic response between thyroid hyperplasia in dogs and in human beings. Results of dieting upon patients with Graves' disease were reported. When butter was added to a normal diet, the symptoms were intensified. There was an increase in basal metabolism, a diminution in weight, and an accentuation of the tachycardia and nervous phenomena. A diet so arranged as to contain a small amount of fat and 15 cc. of cod liver oil daily, with separated milk powder, porridge, bread, green vegetables, eggs and lean meat, yielded a reduction in basal metabolism, an increase in weight, and in a lessening of the tachycardia and restlessness. Working on the assumption that the action of the cod liver oil was

due to the iodine content, 6 to 9 grains of potassium iodide were given to some patients instead of the oil. After a period of reduced basal metabolism, the weight of these patients became stationary or fell slightly.—I. B.

(THYROID) Idiopathic MYXEDEMA in a man of 37 (Idiopathisches Myxödem bei einem 37-jährigen Mann). Meyer-Bisch, Klin. Wchnschr. (Berl.), 1922, 1, 1765.

The disease began when the patient was 14. Treatment with thyroïdin gave splendid success. The patient lost 37 kg. weight and his psychical functions rapidly improved.—J. K.

THYROID extract and experimental lesions of nutrition (Extrait thyroïdien et lésions de carence expérimentale). Mouriquand (G.), Michel (P.) & Sanyas (R.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 214-215.—T. C. B.

Diets adjuvant and antagonistic to the dystrophic action of THYROID extracts (Les régimes adjuvants et antagonistes de l'action dystrophique de l'extrait thyroïdien). Mouriquand (G.), Michel (P.) & Sanyas (R.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 216-218.—T. C. B.

A case of THYROIDEAN strumous teratoma of the OVARY (Un caso di teratoma strumoso tiroideo dell' ovaio). Parodi (A.), Pathologica (Genova), 1922, 14, 727-731 (November).

The author considers ovarian struma as a teratoma in which the thyroidean tissue is the only constituent or is more or less abundant according to the predominant development of the cells of either layer. He believes that the tumor is malignant or not according to the quality of its tissue. He claims that "ovarian struma" is too generical a term and prefers to follow the nomenclature of Norris and Proescher and call it "thyroidean strumous teratoma of the ovary."—G. V.

Studies in the Kottmann reaction for THYROID activity. Petersen (W. F.), H'Doubler (F. T.), Levinson (S. A.) & Laibe (J. E. F.), Arch. Int. Med. (Chicago), 1922, 30, 386-396.

The author's conclusions, which adequately summarize the article, are as follows. In clinical cases of hyperthyroidism the Kottmann reaction may return to normal after thyroidectomy. On the other hand, he produced a positive reaction in two patients; in one, a normal control patient who were subjected to similar trauma, but who were not frightened (one unconscious, one semi-conscious, the other conscious and calm), the reaction was within normal limits. Experimentally it was found that thyroxin injection, irradiation and massage of the hypertrophied gland resulted in an increased protective property of the serum which becomes

manifested in the course of several days. The serum alteration is therefore not a direct one, but is evidently the result of alterations in cellular metabolism brought about by the increased thyroid activity. Other experimental procedures may alter the reaction (bacterial shock, peptone shock, trypsin ingestion, hemorrhage, irradiation of remote organs). In no case was the delay in the reaction comparable to that observed with exophthalmic serums and we do not believe that the alterations in the reactions observed under these experimental conditions will detract from the clinical usefulness of the test in the diagnosis and the control of the therapy of thyroid dysfunction.—H. L.

The Kottmann reaction for **THYROID** activity. Peterson (W. F.), H'Doubler (E. T.), Levinson (S. A.) & Laibe (J. E.), Tr. Chicago Path. Soc., 1922, 11, 261-263.

See Endocrin., 6, 740.

(**THYROID**) Case of laryngectomy following thyro-issure. Ridout (C. A. S.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 8-9.

Description of the case of a male, aged 51, in whom, at operation for carcinoma of the larynx, it was discovered that the left lobe of the thyroid was involved.—I. B.

The action of **THYROXIN** on the body weight and liver glycogen of the mouse (Untersuchungen über die Wirkung des Thyroxins. I. Ueber die Wirkung des Thyroxins auf Körpergewicht und Leberglykogen weisser Mäuse). Romeis (B.), Biochem. Ztschr. (Berl.), 1923, 135, 85-106.

The general conclusion derived from this study is that thyroxin produces effects on body weight, fat tissue and liver glycogen entirely analogous to those produced by thyroid gland administration. Certain differences in sensitivity to the compound were found in the various mice used which were not attributed to age, sex or weight differences.—F. S. H.

The rôle of the **THYROID** in anaphylaxis (Quelques remarques au sujet des notes présentées par L. Kepinow et A. Lanzenberg sur le rôle de la glande thyroïde dans l'anaphylaxie). Savini (E.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 235-237.—T. C. B.

The influence of partial ablation of **THYROID** and **THYMUS** (Über die Wirkung partieller Entfernung von Thyreoidea und Thymus). Scheunert, Klin. Wchnschr. (Berl.), 1922, 1, 1625.

In rabbits neither removal of half of the thyroid nor grafting of the thymus had any influence. In a young pig this operation, combined with castration, augmented the growth rate and increased the quantity of fat. Control experiments showed that whether the thymus was grafted made no difference in the results. The weight

of the animals that had been operated upon and of the controls became similar at the 100 kilogram stage. In one pig half of the thymus was removed; the animal became stupid and acquired thick skin, thick ears and long hairs.—J. K.

(THYROID) Studies of nephritis in children. I. Nephrosis. Schwarz (H.) & Kohn (J. L.), *Am. J. Dis. Child.* (Chicago), 1922, **24**, 125-159.

Epstein and Lande showed that in this type of nephritis the basal metabolism is lowered very much below the normal. As the patients improve, the basal metabolism approaches nearer the normal. The metabolism is always low when the cholesterol is high, and high when the cholesterol is reduced in amount. Schwarz and Kohn report that the use of thyroid extract seems to raise the basal metabolism in these cases and in many instances has a miraculous effect on the edema. They began their treatment with small doses of thyroid and controlled the increase by basal metabolism determination.—M. B. G.

Adenomata of the THYROID. Shephard (J. H.), *California State J. M.* (San Fran.), 1923, **21**, 16-18.

The repair and activation of the THYROID in the HYPOPHYSECTOMIZED tadpole by the parenteral administration of fresh anterior lobe of the bovine hypophysis. Smith (P. E.) & Smith (I. P.), *J. Med. Research* (Boston), 1922, **43**, 267-283.

The authors have investigated in the pituitaryless tadpole the structural and functional responses of the thyroid to injections of fresh bovine pituitary substance. Studies previously carried out on this form have shown that when the buccal hypophysis is ablated at an early stage the thyroid becomes atrophic and functionally inactive. These animals do not metamorphose. This failure of the thyroid has been corrected by the injection of anterior lobe substance; injections of the neural or intermediate lobe do not repair the gland. With a moderate dosage of anterior lobe substance the atrophic thyroid can be brought to a normal size (as determined by wax models) and structure, the specimens metamorphosing. With larger doses or with more certainty when only the middle part of the anterior lobe is used the thyroid becomes relatively enlarged and exhibits pronounced hyperplasia. Thus by varying the anterior lobe hormone it is possible to secure any type of thyroid from one displaying extreme atrophy to one displaying pronounced hyperplasia. The feeding of anterior lobe does not affect the thyroid. General body overgrowth and a pronounced darkening resulted from these injections in both the hypophysectomized (albino) and normal tadpole.—Author's Abst.

(THYROID) Graves' disease, its pathogenesis and its treatment (De zichte van Basedow haar pathogenese en haar behandeling). de Stella, Vlaamsch. geneesk. Tijdschr. (Gent), 1922, 3, 658-664.

A general review without new data, offering inadequate evidence that Graves' disease is caused only by inflammation of the throat. The importance of emotions is denied.—J. K.

THYROXIN, its history, chemistry, and therapeutics. Stephenson (T.), Prescriber (Edin.), 1922, 16, 334-339.

No new data.—F. C. P.

(THYROID) The metamorphosis of neotenus amphibians. Swingle (W. W.), J. Exper. Zool. (Phila.), 1922, 30, 397-422.

Necturus does not undergo metamorphosis when fed, injected or engrafted with thyroid substance. The physiological activity of the thyroid substance used was demonstrated by using it on immature larvae of *Rana clamata* which underwent premature metamorphosis. Thyroids are present in necturus and may be shown to be physiologically active when engrafted into immature anuran larvae. It is evident that necturus has lost the power to metamorphose in response to stimulation by thyroid administration. Axolotl, on the other hand, responds readily to feeding or injection of thyroid. Axolotl possesses a large thyroid which, although incapable of producing metamorphosis in the animal itself, has a stimulating effect on the immature larvae of anurans. The same is true of the thyroids of large neotenus larvae of *Rana clamata*, which stimulate immature larvae of the same species. Four explanations are suggested for the failure of the thyroid to cause metamorphosis in these neotenus forms. They are: (1) defective blood supply for taking away the hormone; (2) a defect in the nervous stimulation which makes it impossible for the gland to release the hormone into the blood stream; (3) defective endocrine interrelations which prevent the release of the hormone; (4) or the presence of substances in the blood which neutralize the hormone.—M. M. H.

THYROID transplantation and anuran metamorphosis. Swingle (W. W.), J. Exper. Zool. (Phila.), 1923, 37, 219-257.

The thyroids of *Rana catesbeiana* and *Rana clamitans* were transplanted into other larvae of the same species. The two forms used have a very long larval life and the object of the experiments was to determine the time at which the thyroids of these species become physiologically active. Glands were selected for transplantation at different periods of the larval life. It was found that while the thyroids of immature larvae do not cause an acceleration of development in the host, those from specimens having fairly well developed hind limbs will cause a slight hastening of metamorphosis and those from newly metamorphosed frogs will cause a greater

(**THYROID**) Graves' disease. Waller (H. E.), Prescriber (Edin.), 1922, 16, 323-327.

The author concludes from his experience with 70 cases that Graves' disease is determined by the endocrine make-up of the individual (largely a hereditary matter), that it is usually secondary to some chronic infection, such as dental defects, tonsillitis, chronic nasopharyngeal inflammation, rheumatism, colonic disturbance, or tuberculosis. Waller believes that surgery and x-ray treatment are necessary only in exceptional cases.—F. C. P.

(**THYROID**) Graves' disease and fibrinous bronchitis (Basedow'sche Krankheit und Bronchitis fibrinosa). Weber (H.), Med. Klin. (Berl.), 1921, 17, 1143; abst., Schweiz. med. Wchnschr. (Basel), 1923, 53, 127.

A case report. The author believes that vagus hyperirritability played an important part.—R. G. H.

Surgery of THYROID. White (P. A.), Iowa State M. Soc. J. (Des Moines), 1923, 13, 11-15; cit., J. Am. M. Ass. (Chicago), 1923, 80, 656.


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THE SOURCES OF ERROR IN ORGANOTHERAPY AS ILLUSTRATED BY THE PREPARATION AND ADMINISTRATION OF INSULIN*

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During the past two years, our knowledge of organotherapy has been greatly enriched by the discovery of the new anti-diabetic hormone, insulin, by F. G. Banting (1) and his associates of the University of Toronto. During the past fourteen months, all of our research activities have been devoted to the preparation and clinical use of this new endocrine substance. We are presenting this paper in the hope that the lessons we have learned in the preparation, the standardization and the use of this new product may point out some of the probable sources of error in this and other types of organotherapy.

All will agree that: (1) an endocrine product should contain the active principle which it is supposed to contain; (2) that methods of standardization should be devised whereby the amount of such active substance may be accurately measured; and (3) that such substances should be administered by

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routes which will insure their absorption in a sufficient degree to produce the desired physiological effects.

Since the discovery of Von Mering and Minkowski that the total extirpation of the pancreas resulted in early, fatal diabetes and the subsequent work which led investigators to believe that the islands of Langerhans elaborated an internal secretion which was either directly or indirectly responsible for the proper carbohydrate metabolism, pancreatic extracts in many forms have been tried. Previous to the work of Banting, no convincing results were obtained. We now know that these failures were probably due to the fact that none of these preparations contained much if any of the active principle now known as insulin. Banting theorized and proved conclusively that this was due to the early, rapid destruction of insulin by the proteolytic enzymes of the acinar cells of the pancreas. He circumvented such action by the ligation of the pancreatic duct in dogs, following which procedure the acinar cells degenerated in from seven to ten weeks. From such degenerated glands, he made small quantities of impure but potent insulin extracts. Collip (2) then worked out the present method of circumventing the action of these destructive enzymes by inhibition and precipitation with alcohol. Such extracts made from adult ox pancreas were also found to be active in diabetic dogs and when a sufficient degree of purity and potency had been obtained, they were tried with convincing results on patients suffering from diabetes.

The production on an economical scale of potent extracts of insulin, however, does not depend entirely upon the circumvention of the action of the proteolytic enzymes, although this must be considered the first essential and great care must be taken in excising the glands as rapidly as possible and chilling them at once to preserve the insulin through the first steps in the process. The glands from recently and well fed animals probably give a higher yield than the glands from poor and previously starved animals. The yield is materially increased by the use of the hydraulic press. In filtering off the precipitated enzymes, much of the insulin may adhere to the precipitate unless the extract is permitted to stand a day or two.

before filtration. In certain stages of the removal of the alcohol by vacuum distillation, prolonged heating at moderate temperature is injurious. The hydrogen ion concentration must be watched at all stages. Variations in the hydrogen ion concentration no greater than that between distilled water and tap water spell marked success or partial failure. The process is by no means perfected but by attention to such minor details we have been able to increase our yields many fold.

The Toronto group next devised a method of testing solutions on rabbits enabling them to arrive at comparative degrees of potency. When insulin is given hypodermically or intravenously to rabbits, the blood sugar falls and if the fall is sufficiently great, convulsions occur.

Patents on insulin were applied for and obtained by Dr. Banting and turned over to the University of Toronto. Temporary rights to manufacture a commercial supply of insulin were granted to Eli Lilly and Company of Indianapolis, Indiana, and various research laboratories were permitted to assist in the development of the problem. The Eli Lilly unit is the amount of insulin necessary to produce a convulsion in a one kilogram rabbit in the course of four hours following a subcutaneous injection. In our own experience, such units have a sugar-metabolizing power of a little more than one gram of glucose.

It may not be out of place here to record a word of commendation for the truly scientific endeavors that Eli Lilly and Company have put forth to produce a proven high grade product. For months, and without charge, they furnished large quantities of this precious extract to recognized diabetic clinics, seeking nothing in return except an opinion as to the patient value of their unit. If other manufacturers would exercise the same care, the endocrine problems would be much more rapidly solved.

We know that insulin is efficacious when given subcutaneously and intravenously, but for months we have failed to obtain any effects by alimentary administration. We have given it in coated and uncoated capsules and in various solvents in amounts exceeding twenty-five times the subcutaneous convulsion

dose with no effects on the blood sugar. The problem is still being investigated.

Eli Lilly and Company's Iletin is therefore a potent product of known physiological strength that must be given hypodermically.

There are a large number of pancreatic extracts on the market intended for alimentary administration which are said by the manufacturers to contain a substance or substances of specific value in the treatment of diabetes. The value of these products is not supported by careful scientific investigation but by testimonials from physicians and patients. We have examined three of the best known of these preparations with the following negative results.

Two lots of pancreatic compounds were submitted by the Harrower Laboratories of Glendale, California. Insofar as we could determine, neither of these products contained any of the substance we now know as insulin. Water extracts of these products had no effect on the rabbits' blood sugar when given intravenously, subcutaneously or orally. They did contain proteolytic enzymes which we now know are incompatible with the coexistence of insulin. We promptly reported our results to the Harrower Laboratories but received no reply.

We examined a pancreatic extract furnished by the G. W. Carnrick Laboratories of New York with identical results, and later they sent us some enzyme-free pancreatic extract which was enzyme-free but produced a rise rather than a fall in the blood sugar of rabbits.

At our request, Armour and Company of Chicago sent us a supply of their insulase in capsule form for oral administration which was then (February 19, 1923) being advertised in the Journal of Biological Chemistry and other journals. This product from the similarity of the name to insulin and because of the advertising media used, we expected would contain insulin. As before, insofar as we could determine by similar animal experimentation, these capsules contained no insulin. Twenty capsules in a single dose were taken by one of us on a weighed diet with no effect. These capsules also contained proteolytic enzymes.

THE PRESENT STATUS OF OUR KNOWLEDGE OF THE OTHER
ENDOCRINE GLANDS

The Adrenals. The adrenal gland consists of two parts, the cortex and the medulla. Very little is known about the function of the cortex except that it bears some relation to the development of the sex glands originating embryologically from the mesoderm as do the sex glands. The cells are very similar to those of the corpus luteum. In sexual precocity the adrenal cortex is hypertrophied. Tumors of the cortex probably associated with hyperfunction in young children are associated with the premature development of the secondary sexual characteristics. A boy of four or five years may have the sexual development of a mature male. In female children, the breasts hypertrophy, hair appears on the mons veneris, the uterus matures and menstruation may occur. The cortex hypertrophies during pregnancy and after castration. It is ill developed in sexual deficiency. It is believed that it is the cortex and not the medulla which is essential to life since $\frac{7}{8}$ of the gland may be removed provided the portion left is cortex. No proved extracts of the cortex have been made and this important field of organotherapy is open for investigation.

Adrenalin is, in all probability, an extract of the medulla. The active principle of this extract has been isolated in crystalline form by Takamine and Abel. Much of the present commercial supply is made synthetically. Its strength is well standardized. Sansum and Woodyatt (3) have shown that preparations in the large containers such as ounce bottles soon deteriorate after the bottles are opened, so that unless this product is being used in comparatively large quantities, the 1 cc. ampules give the most dependable results. Except on mucous membranes such as the nose and throat, adrenalin is apparently of no value, unless given intravenously or hypodermically. The rôle which adrenalin plays naturally in the body is still a much debated and certainly an unsettled problem.

The Thyroid Gland. Insofar as known, the thyroid gland is anatomically alike throughout. Its active principle, thyroxin, has been isolated by Kendall (4) and its chemistry is known.

This principle, when given by mouth, is a specific in the treatment of hypothyroid conditions. It is a noteworthy fact that thyroxin is the only one of the endocrine products that is surely absorbed by way of the alimentary tract and that in the beginning it was feared that this could not be done. The degree of thyroid deficiency or over-activity may be determined by basal rate determinations. These basal rate determinations also furnish an excellent method of actually determining whether a sufficient dose has been given. The experimental preparation of thyroxin was attended with fully as many difficulties as we are now meeting in the preparation of insulin, and it is well known that many of the typical preparations on the market have very substandard values in proportion to the amount of original gland substance used.

The Parathyroid Gland. Here again, we have an unexplored field. Extirpation of the parathyroid gland is rapidly followed by death associated with tetany. Disease of the parathyroid glands probably associated with hypofunction, results in rapid emaciation, failure of growth, disturbances in the carbohydrate metabolism and, most definite of all, an interference in the calcium metabolism as illustrated by the failure of the teeth and bones to calcify properly. Such conditions have been improved by transplantation of parathyroid tissue from patients who have died. Luckhardt and Goldberg (5) have shown that parathyroidectomized dogs can be kept alive if large amounts of calcium lactate are given by mouth. Also Dragstedt (6) has secured similar results by means of aciduric diets (milk, lactose, etc.), thus causing detoxification. No proved extracts have as yet been made.

The Pituitary Body. The pituitary body consists of two parts, the anterior lobe and the posterior lobe. The pars intermedia is usually included with the posterior lobe. The active principle of the posterior lobe, pituitin, is in some respects similar to adrenalin.

The Anterior Lobe. Extirpation of the whole gland is fatal in two or three days. Here, as in the extirpation of the whole adrenal gland, it is probably the extirpation of the anterior lobe which is injurious to life. Decrease in function of the anterior

lobe is associated with lack of development. The subjects become fat and there is depression in the respiratory exchange. Clinical types were first described by Frölich and are grouped under the term, *dystrophia adiposogenitalis*. Increased activity is associated with gigantism or acromegalia. An active principle of the anterior lobe called tethelin has recently been isolated by Robertson (7) and is said to accelerate growth in young animals. Similar effects are said to have been produced by the subcutaneous and oral administration of fresh extracts of the whole gland.

Certain manufacturers of glandular products offer as high as \$8.00 per pound for pituitary bodies. One of us (S) observed the removal of such glands at the slaughter house. The glands are permitted to lie carelessly about on the heated killing-floors and if the active principle has any similarity to other delicate endocrine products we would assume that the active principle could be easily lost before the first step of the extraction was begun.

Posterior Lobe. Pituitrin is thought to be the extract of the pars intermedia and the posterior lobe. This portion of the pituitary body can be removed with so little functional change that very little can be learned concerning the function of this part by this method.

Pituitrin has an action somewhat like adrenalin. A crystalline form has been obtained but this is thought to be a mixture of various substances.

The Pineal Gland. Very little is known about the pineal gland. When removed in the fowl, the body growth is said to be stimulated and the sexual characteristics develop more quickly. The same conditions occur in tumors and following administration of the gland substances, which makes such results hard to interpret.

The Gonads. The results of castration are well known. These glands are supposed to have a double function, that of the elaboration and secretion of the spermatozoa and secretion of a substance from the interstitial cells. The isolation and study of this internal secretion is another one of the open fields for investigation. We fully believe that such a secretion exists but

the results of the injection of testicular extract on the development of sexual characteristics in different animals is still considered as having a negative value. It may be that such extracts do not contain the active substance they are supposed to contain.

The Female Generative Organs. The results of spaying are well known. They are not so pronounced as the results of castration. The ovary is supposed to have at least a triple function: (1) ovulation, (2) secretion of a substance from the interstitial cells which is supposed to be somewhat similar to the secretion from the interstitial cells of the testicles, and (3) a secretion of a substance from the corpus luteum. Nothing definite as yet has been proven concerning the secretion of the interstitial cells. Extracts of the corpus luteum have been made. This secretion when given intravenously has a pituitrin-like action. The active principle has never been isolated, and there is no definite proof that the impure substance is of any value when given orally. On this point, there is considerable clinical dispute, some clinicians claiming excellent results during the disturbances incident to the menopause, and others claiming just as good results by hygienic measures alone.

The Thymus Gland. The thymus is essentially a lymphatic gland and the proof that it has an internal secretion is entirely wanting.

It seems to us that any experimental work on an endocrine product should begin with the isolation of a substance or substances that have a proved physiological value, that the degree of such potency should be determined and that the route or routes of administration should be proved.

CONCLUSIONS

In this paper we have summed up our experiences in the preparation and administration of probably one of the most important and longest sought for endocrine products of the body. Work on this product must be considered just begun. We have pointed out the difficulties attendant to its extraction, the efforts now being made toward its standardization, and the fact that thus far other than hypodermic or intravenous methods of administration have been failures. We believe that organo-

therapy in general has a wonderful future, but we also realize that its future development will depend not upon empirical, haphazard methods of study but upon the type of study which has led to our present knowledge of such products as adrenalin, thyroxin, pituitrin and insulin.

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THE INSULIN CONTROL OF DIABETES MELLITUS AND ITS COMPLICATIONS*

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The insulin treatment of diabetes mellitus made possible through the discovery of Banting and his associates, including Macleod, Best, Collip and others of the University of Toronto, occupies the center of attention in the medical world today. Joslin writes in a recent article, "The contribution of Banting and Best to the treatment of diabetes is greater than I ever expected to witness." All diabetic specialists, including Allen, Joslin and Woodyatt have incorporated insulin into their treatments and can confirm the original conclusions of the Toronto group that with the use of insulin even the most severe diabetics can be restored to health and strength.

In our discussion of the insulin treatment of diabetes mellitus, it must again be emphasized that it is not a cure for the disease. This fact, however, does not detract from the marvelous importance of insulin. The low calory diets which were formerly used in the treatment of the severe cases are now unnecessary. Under-nutrition to render patients sugar free is no longer in order, for insulin makes possible the consumption of enough carbohydrate to completely metabolize a reasonable amount of protein and sufficient fat to supply the caloric requirements of patients. Infections no longer are the source of great danger to diabetics, and surgery can be done with the assurance that the severe acidosis so often resulting can be readily controlled by intelligent insulin therapy. Finally, patients in severe acidosis and early coma can usually be saved by the use of insulin.

TREATMENT

All diabetics, whether having a mild or a severe case, need the thorough training in the dietetics necessary for insulin treatment. Subjects of mild as well as severe diabetes should be able to prepare a menu and estimate their diets according to

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their tolerances in grams of carbohydrate, protein and fat. If insulin is to be used, this is absolutely necessary. For patients who are unable to compute such a diet a compromise with rigid diets of known food values must be granted. Insulin is necessary for all diabetics whose carbohydrate tolerances do not allow sufficient caloric intakes to keep them strong and well. Small doses of insulin, however, may be of benefit even in mild diabetes, helping to arrest the downward progress of the disease and activating the general metabolism of the body in a manner difficult to explain but evident from a clinical point of view.

Physicians who undertake the insulin treatment of diabetes mellitus must therefore understand the mathematics of dietetics and be able to prescribe diets of a constant carbohydrate, protein and fat content or, better still, be able to teach their patients how to arrange varied diets of constant values. These diets must be balanced in relation to carbohydrate, protein and fat according to the generally accepted ideas concerning ketone destruction. Physicians who use insulin should be able to conduct the various tests commonly used in the study of diabetes, especially that for blood sugar. They should keep in touch with their patients and be able to adjust diets and insulin dosage in case tolerances increase or infections occur. Careful histories, physical examinations and blood sugar determinations should precede all insulin therapy and renal diabetes must be excluded. Finally, foci of infection must be searched for and, if found, should be removed only after the diabetes is under insulin control.

INSULIN ADJUSTMENT

If the diabetic is unable to metabolize a diet sufficient to maintain weight and strength for the occupation he must pursue, insulin should be administered. The dose may be determined in the following way: the available carbohydrate of the required diet can be determined by adding to the grams of carbohydrate in the diet the other sugar formers which, as Wood-yatt has emphasized, consist of 59 per cent of the protein and 10 per cent of the fat; the difference between this result and the number of grams of glucose excreted in the 24-hour period gives the natural glucose tolerance for the patient. McPhedran and Banting recently state that one unit of insulin will utilize from

one gram of carbohydrate in the severe cases, to 2.5 grams in the mild cases. It is well to assume the maximum effect when insulin therapy is to be begun, and the 24-hour dose can be estimated by dividing the number of grams of glucose in the 24-hour urine by 2.5. For physicians not accustomed to the use of insulin, even a smaller dose might be advisable, as suggested by Joslin. Further 24-hour glucose determinations indicate the necessity of increase in insulin, or reduction in diet, in order to render the patient sugar free.

We have usually been able to divide the insulin requirement for the 24 hours into two doses, approximately three-fifths being given one-quarter to one-half hour before breakfast and two-fifths at the same time before the evening meal. Slight differences in the relative amounts of insulin given and the time of injections may be necessary. A few patients require a small noon dose, though with a large morning injection the blood sugar is usually low enough at noon to allow the ingestion of a meal without insulin. The evening dose must not be so large that the blood sugar is depressed during the night with insulin reactions developing during sleep. It is important, moreover, to vary the site of injection. Several irregular actions of insulin in our experience were found to be due to its irregular absorption, resulting from the continual injection of the extract in the arms. Moderate tissue irritation at times occurs in our patients, but no infection has resulted in over ten thousand injections to date. Mild urticaria at the site of injection or more general urticaria occasionally appears within one to two weeks after the first hypodermics. Calcium lactate has been given to such patients with relief.

During the period of desugarization by insulin, frequent examinations of single specimens of urine should be made, especially if full doses of insulin are being administered. When a few grams of sugar persist in the 24-hour specimen, examination of single specimens will show when the sugar is being excreted, and insulin can be increased in the dose preceding such glycosuria. The possibility of a residual urine or retention of urine in semi-comatose or completely comatose patients must be remembered. In such cases frequent catheterized specimens, only, can reveal the true analysis of the urine. Thus for accurate work, frequent blood sugar determinations are desirable while

the patient is becoming sugar free and during the period of insulin adjustment.

Whether it is advisable to allow a slight hyperglycemia during insulin treatment is a question. Hypoglycemia is certainly to be avoided. Personally, however, it seems to me better to maintain a normal or even slightly elevated blood sugar to obviate any insidious effects from long continued hyperglycemia and to make the patient as normal as possible.

During the first few weeks after the patient is sugar free a rapid increase in natural tolerance may occur, indicated by the lowering in the blood sugar level or by insulin reactions. In such cases insulin must be decreased or even stopped for a dose or two and the diet raised until a constant equilibrium between diet and insulin is reached.

DIET ADJUSTMENT

The proper balancing of the carbohydrate, protein and fat in the diet must be discussed. My own experience confirms the opinion of Newburgh and Marsh in regard to the use of high fat diets. These diets are still necessary in many severe diabetics in order to be economical with insulin and to give enough calories for activity. I feel that it is desirable but unnecessary to keep the ratio of fatty acid formers, that is, 46 per cent of the protein plus 9 per cent of the fat to the glucose formers; that is, 100 per cent of the carbohydrate plus 58 per cent of the protein plus 10 per cent of the fat, below 1.5 or even 2, as Wilder suggests. The work of Shaffer, especially, makes these ratios appear too conservative. We agree with Joslin in feeling fortunate not to have invented a diet formula and to be able to take the best from all systems. Thus in regard to protein, we plan to give about one gram of protein for each kilogram of the normal weight of the patient. This amount has been shown to assure a positive nitrogen balance, and is not so large that an excess of acid formers and too much specific dynamic action on the basal metabolism results. From one and a half to three times as many grams of fat as available carbohydrate are added to the diet, according to the caloric requirements of the patient. The total calories are thus increased so as to maintain or attain a normal weight. Boothby and Wilder have shown that for ordinary activity 20 to 30 per cent more calories than the basal requirement are necessary.

CLINICAL EXPERIENCE

In order to illustrate the above method of instituting insulin therapy, the data on a severe diabetic recently treated with insulin is given in Table I. D. L. was first seen by me one and a half years ago, two weeks after the sudden onset of diabetes. In spite of urgent advice, treatment was not continued. Lately,

TABLE 1

Date	DIET			Available G	Urin- ary G	Nat'l G Toler- ance	URINARY		BLOOD		Gms. of G Equiv. to 1 H	Insulin (Lilly)	Remarks
	C	P	F				NH ³	Dia- cetic	CO ² Vol. %	Blood Sugar			
May 22	45	75	150	103	130	-27	7.4	+++	37	.435		0	Drowsy, weak, boil on arm.
23	45	75	150	103	99	+4	5.3	+++				0	
24	45	75	150	103	29		4.8	+++	48		1.8	40 H	
25	45	75	150	103	21		4.7	+++			2.0	40 H	
28	45	75	150	103	12		2.9	++			1.8	50 H	
29	39	75	150	97	8		2.5	++	56		1.8	50 H	
30	39	75	150	97	7			+				50 H	
June 1	33	75	150	91	2			0			1.8	50 H	
2	33	75	150	91	0			0				50 H	
3	33	75	150	91	0			0				50 H	Slight insulin re- action.
4	36	75	150	94	0	12	1.3	0				49 H	Slight insulin re- action, 6 gm. of sugar taken.
5	42	75	150	100	0	25		0		.164		45 H	Slight insulin re- action, 6 gm. of sugar taken.
6	42	75	180	103	0	38		0				37 H	Slight insulin re- action, 6 gm. of sugar taken.
7	42	75	180	103	0	50		0				35 H	Marked reaction, 10 gms. G.
8	45	75	180	106	0	54		0				32 H	Slight reaction, 6 gms. G.
9	48	75	180	109	0	57		0				32 H	Slight reaction, 6 gms. G.
10	54	75	180	115	0	57		0				32 H	No reaction.
11	54	75	180	115	0	57		0		.151		32 H	Feels well and strong.

D. L., aged 28, weight 180, height 5 ft. 9 in. Diabetes of two years. Gradual increase to extreme severity shown above with marked acidosis. Aggravated by large boil: Glycosuria, hyperglacæmia and acidosis controlled by insulin alone.

he had been weak, drowsy and irritable, and a severe boil had developed on his arm, which had aggravated his diabetes. From his clinical condition and the data presented it is evident he was approaching coma.

In spite of severe acidosis he was placed on a low maintenance diet of 1800 calories at the start. Fat was not reduced and insulin was given immediately. Assuming that one unit of insulin (Lilly) would metabolize a maximum of 2.5 grams of carbohydrate, 40 units (II) were ordered during the first day of insulin therapy. It was found, however, that only 1.8 grams of carbohydrate were taken care of by each unit of insulin. This result was confirmed on several successive days, and may be accepted as this patient's carbohydrate equivalent for one unit. He gradually became sugar and acid free, and his sense of well being and normal mental reactions rapidly returned. After becoming sugar free, his natural tolerance increased so that within three weeks it had risen from 0 to around 60 grams of glucose formers.

The data on Miss A. F. are given in Table II to indicate a more rapid method of handling severe cases of diabetes. This girl was extremely weak and drowsy, and I wished to get her acid and sugar free quickly. The first dose of insulin of 10 H was given at 4 P. M. and in 2 hours this dose was repeated and some oatmeal gruel was given. Water was forced by mouth and frequent urinalyses were made. By 9 P. M. the urine was both acid and sugar free. The blood sugar was immediately analyzed and because of its normal value and the possibility that the insulin was still lowering the blood sugar level, 60 cc. of orange juice was prescribed. The patient was watched carefully during the night and no insulin reaction occurred. One unit of insulin was ordered for about every two grams of available carbohydrate in the diet for the following day. The diet was rapidly increased and the insulin decreased according to clinical indications and blood sugar determinations. A splendid gain in weight and strength took place within three weeks time.

Insulin has been administered to seventy-five patients exclusive of those in coma during the last seven months in our clinic. Twenty-seven of this number have been placed on 20 to 45 units daily and forty-seven are taking from 3 to 20 units a day. Six patients are in the first decade, four in the second,

four in the third, seventeen are between the ages of thirty and fifty, and forty-four between the ages of fifty and eighty-five. Most patients are having insulin administered at home, either by themselves or by some person in the household. There has been a universal improvement in the clinical conditions in all patients, most marked in the children and young adults and less so in a few of the patients over sixty. Weight has increased

TABLE 2

Date	DIET				Insulin	URINARY			Blood	Weight	Remarks
	Cha.	Prot.	Fat	Cal. Per Kg.		Sugar	Dia-cetic	NH ³	Sugar		
Mar. 31	Mod. Breakfast	limited	tion for lunch		20 H	2.6	+++	3.0		89	Weak, nervous, depressed, drowsy.
P.M. 4:15	Treatment	begun			10 H	+++	+++		.277		Green vegetables and meat for 2 weeks.
6:00	10	2.5	1		10 H	++	++				Restricted diet for 3 months.
7:00						+	+				
9.00	6	(Orange juice)				0	0		.122		
April 1	40	43	57	21	32 H	0	0	1.2	.077		No insulin reaction.
2	45	45	75	25	30 H	0	0	1.3	.112		Sitting up in chair, stronger.
7	45	60	150	43	22 H	0	0		.165	91	Left hospital, walking.
14	45	60	150	39	22 H	0	0			100	Feels perfectly well.
23	45	60	150	37	22 H	0	0		.154	104.5	Feels stronger than for months.

Miss A. F., diabetes of 10 months duration. Acute onset, loss of 30 lbs. in weight. Age 18 years.

in nearly every case, in one instance amounting to fifty pounds. Complications such as neuritis, neuralgia, paresthesias and retinitis have in most instances improved under persistent therapy.

INFECTIONS

It is important that simple food, containing the usual number of grams of carbohydrate, protein and fat, be taken along with insulin during infections. Diabetics must continue to be fed during these periods and as the glucose tolerance usually diminishes, insulin must frequently be given in larger doses than

usual. This increase in dose can be determined by quantitative glucose determinations in the 24 hour urine. If the caloric intake is reduced insulin may also be cut down as determined by urinary and blood examinations. If nausea or indigestion occur an emetic should be given and the bowels emptied by castor oil, after which simple carbohydrate, protein and fat mixtures should be prescribed as soon as the stomach will tolerate them. If for any reason it is impossible to give food by mouth, 10% glucose by vein will make possible the continuance of insulin therapy and thus prevent the onset of a severe acidosis. Subjects having only a mild form of diabetes who usually do not need insulin will often require it during infections. We have seen erysipelas, carbuncles, boils, sinusitis, pneumonia, phlebitis, appendiceal abscesses as well as other infections follow a normal course to complete recovery under insulin treatment.

SURGERY

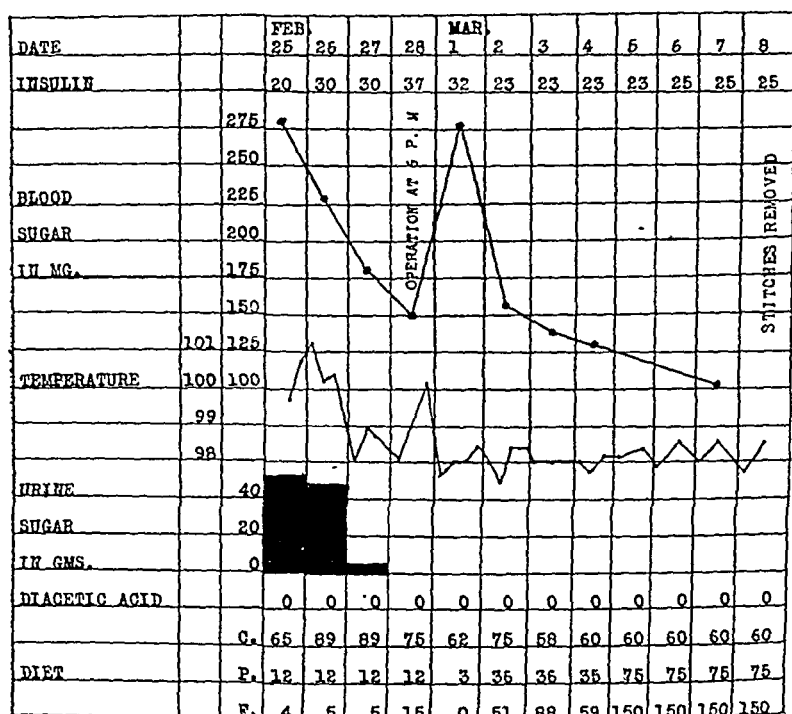
Murphy wrote, "No class of patients is more prone to surgical complications, has less tendency to recover and less resistance to toxic infection than the diabetic." Very few diabetics can undergo an operation and escape a resulting acidosis and a period of decrease in tolerance. Insulin, however, can take care of both of these serious results and as a consequence the surgical mortality in diabetics in the future is going to be greatly reduced. However, no surgery should be attempted except in an emergency unless the patient is under the dietary and insulin control of a physician skilled in diabetic treatment. After operation, fluids should be forced and 10% glucose administered by vein in proper amounts as long as food is withheld by mouth. Insulin must be continued and the dose carefully controlled by blood and urine analyses.

During the last few months we have controlled the post-operative period with diet and insulin in the following surgical conditions: three high amputations of the leg because of gangrene of the foot, one amputation of a toe due to gangrene, two carbuncles, two ruptured gangrenous appendices, one thyroidectomy, and one extensively infected hand following amputation of an infected finger. There has been only one death and that in an amputation in a woman of seventy-six years, whose incision healed perfectly in ten days and who died two weeks

after operation, of a general physical and mental failure associated with her age.

Chart III shows the rapid control of diabetes in a man of seventy-six with gangrene of the foot who suddenly developed a gas infection in his leg and who after an emergency operation was immediately free from all pain and fever and made a rapid recovery in ten days time.

CHART 3



DR. O. L. AGE 76. DIABETES OF 20 YEARS. GANGRENE OF 2 MONTHS. RAPID EXTENSION FOLLOWING AMPUTATION OF TOE WHEN PATIENT WAS NOT SUGAR FREE. EMERGENCY HIGH AMPUTATION BECAUSE OF SUDDEN GAS BACILLUS INFECTION. NO PAIN OR TEMPERATURE.

COMA

Theoretically coma should not occur, especially since we now have insulin. But as long as patients refuse to let reputable physicians treat diabetes, and until the physicians at large realize the importance of recognizing the severe acidosis preceding coma, the actual treatment of this condition will confront the me-

Quick action in the early stages of coma before permanent damage has been done to the vital organs will, with the use of insulin usually save the patient. The general measures emphasized by Joslin such as forcing fluids, keeping the patient warm, washing the stomach of undigested food and the use of stimulants, if necessary, should be carried out. Joslin recently states that as a general rule ten units of insulin every hour for two to four doses and then every other hour for four doses, if necessary, should be given. Certain cases require as much as 100 or more units a day for two or three days, especially if carbohydrate is being administered either by vein or mouth. Recent articles of Foster and Majors report such large doses being necessary in two successfully treated subjects and we have had two subjects in coma that have recovered and that have required similar amounts. These doses consume large quantities of endogenous glucose and thus make possible the burning of the excessive ketones in the tissues.

The treatment must be controlled by blood sugar and urinary sugar determinations. Normal blood sugars are not immediately desirable, though definite lowering is necessary to be sure that ketones are being eradicated.

Three subjects who suffered from diabetic coma and were treated by us with insulin and the general measures outlined above are alive and well today. Two others were completely relieved of their acidosis and died two weeks later, one from a subdiaphragmatic abscess, and the other from a pulmonary embolus. One baby of eight months was brought out of a coma but died of pneumonia within twenty-four hours. One woman of fifty died at the end of forty-eight hours of pneumonia, anuria, and with a blood pressure which persisted around 70 mm. from the beginning of the treatment. One man died within four hours of a ruptured gall bladder. One man of sixty-eight died of a myocardial failure twenty-four hours after he was free from sugar and diacetic acid in the urine and his CO_2 tension had risen to normal.

From our experience in the treatment of coma, therefore, we feel it is most important to prevent the onset of this serious condition and to begin treatment in the early stages of coma if good results are to be obtained.

SUMMARY

The use of insulin is indicated in the treatment of all diabetics who cannot metabolize a diet sufficient to maintain their weights and normal strength. An intimate knowledge of the dietetics of diabetes is important for all diabetics and especially for those taking *insulin*. Every patient must be kept aglycosuric and preferably free from *hyperglycemia*. A practical method of establishing insulin therapy is *outlined* and precautions necessary in its use are *discussed*. The outlook for diabetics who are skilfully treated with insulin and diet during such complications as infection or early coma and when surgery is necessary should be very *favorable* in the *future*.

DISCUSSION OF PAPERS BY DRS. SANSUM AND BLATHERWICK AND DR. ROWE

Dr. Solomon Solis-Cohen, Philadelphia: I consider the paper of Dr. Sansum one of the most valuable contributions that has been made of general suggestions for the use of the secretions as therapeutic agents. Notwithstanding a very long experience with their empirical use and the attempt to formulate rules that might guide me in their administration, I am convinced that the subject is just as Dr. Sansum has said, still in want of a great deal of scientific elucidation, and that while it does not become our duty to abandon the empiric use of organic products, it does behoove us to be very careful in any recommendations that we may make or any conclusions we may formulate and keep to ourselves. The parathyroid gland, for example, is one of those which Dr. Sansum has pointed out as still in want of very considerable study, and no active principle has been extracted therefrom. Nevertheless, one may attempt to use desiccated parathyroid, as many of us have done, and sometimes he will get the result he thinks he ought to have, and very often he will not. The question of failure in the anticipated therapeutic result is three-fold. First, do we actually get parathyroid gland? Second, do we get a parathyroid gland which has been properly prepared? Dr. Sansum has told us what happens to the pituitary. And third, do we get a parathyroid gland, even if properly prepared, which still contains in an active form that substance upon which its physiologic and therapeutic activity depends? I am very much inclined to think that if one has been careful in his therapeutic diagnosis before prescribing the parathyroid gland, the failure is in the product rather than in the intention of the prescriber; but it is a failure nevertheless.

When we do not get failures with parathyroid glands, there is one action which I think ought to be studied much more than any one individual can study it, and that is in the control of certain of the nervous phenomena, and especially those which are expressed in the tremors, not only of the hands, but of other muscles, in exophthalmic goiter.

I have also thought it was useful as an addition to calcium bromide and atropin in the treatment of pyloric spasm in adults, and especially in children. I say I have thought; I do not know. I

know that I have done no harm with it, and I am inclined trying to go on doing some good with it until the laboratories shall give us a refined product to take the place of that we now get in the market.

I think the warning that has been sounded that we must be sure of the product that we get and that we must be sure that it will be absorbed unchanged, or at all events undamaged by the particular route of administration, is highly important. This raises another question. We have been told that the enzymes of the pancreas destroy insulin; but we also know that in the test tubes the digestive enzymes destroy the glucoside of digitalis, and yet we give digitalis by the stomach and we think we get digitalis results. I am not advocating the use of insulin by the stomach; I am using it hypodermically, but it is not at all impossible that some products of the pancreas may eventually be developed which will be capable of use by the gastro-enteric tract, and that will be a great advance.

In regard to insulin: when Banting presented his paper at the Association of American Physicians, I hailed it then as an epoch making discovery, and I do not think the language need at all be altered with the progress of experience. I want to add my thanks to that of Dr. Sansum and the rest to the firm of Eli Lilly & Co., who were very generous in supplying the material for preliminary study of insulin. I am personally very much in their debt for that courtesy.

As to the amount of insulin that is to be used and as to the final effects of insulin, I think there is room for considerable hesitancy in expressing a definite opinion. I am inclined to be much more hopeful today than I was a year ago concerning the ultimate result of the use of insulin in diabetic patients. What I mean may be illustrated by a patient that I saw just before leaving Philadelphia. In the beginning that patient required 40 units of insulin per day to control his glycosuria and his blood sugar within what we considered the reasonable limits upon what I thought to be a necessary diet. After three months of treatment, this subject uses only 5 units a day.

I think we know that the islands of Langerhans are among those structures which are capable of reproduction. We know that the repair and redevelopment of various tissues is not confined to the vegetable kingdom nor to the lower animals, but cell regeneration occurs in man, and I believe that the islands of Langerhans undergo regeneration under rest just as they undergo degeneration under excessive load; and certainly the administration of insulin, if continued under proper conditions, for a sufficiently long time, and if at the same time the patient is properly nourished, will lead to regeneration so that the patient will thereafter furnish his own insulin, as he did at the beginning.

It was my good fortune to have been trained in medicine by the greatest of American physicians since Benjamin Rush, namely, Jacob Mendez da Costa, of Philadelphia. When I heard Dr. Wood and others at meetings in our modern scientific societies bring forth the administration of fat to diabetics as a modern improvement, I could not help thinking of da Costa's words: "When you take away sugar, you have to give fat. The patient has to have something to burn to keep his engine going." You do not feed a diabetic patient or a normal man with calories, you do not feed him with proteins, you do not feed him with carbohydrates nor with fats; you feed him with food. You must analyze the food in order to determine what food is good for the patients in general, or for that particular individual, but what the man wants to know is, "How much rice can I have?" or "How many potatoes?" or "How much bread?" and unless we learn

to estimate our calories and our proteins and our carbohydrates and our fats in terms of articles of diet we will make just as gross an error as does the physician who refuses to estimate his articles of diet in terms of their scientific units.

Anyone who has had much experience with hospitals and in consulting practice will find that there is a type of mind which prefers to turn to a book and get something from the printed page rather than to think it out for himself, and I want in this connection to sound further word of warning. Dr. Joslin and Dr. Allen have published splendid books; we cannot do better than study them, but we cannot do anything worse for our patients than to order Table No. 1 of Joslin or Table No. 12 of Allen, or any other number in any other book. We have to do our own thinking along our own lines and help out our patients by prescribing a diet which he will understand, and the scientific diet for which we will have ourselves estimated.

Dr. N. W. Janney, Los Angeles: In a general meeting of this kind it seems well to emphasize what is, of course, known to the diabetic specialist with great clarity, namely, that an exact dietetic restriction for the diabetic patient is absolutely necessary in connection with the proper use of insulin. We should also bear in mind the matter of under-nutrition. If a patient is found who cannot live comfortably on a scientifically prepared diet, the insulin will permit the use of additional food, hence the practice of under-nutrition can be permanently discarded.

One of the most important aids afforded by insulin is that it has permitted us to simplify the rather severe technique of the diabetic diet. At present I am using but two diabetic diets, one a high carbohydrate diet for combatting acidosis or a precomatose condition; and then afterwards, when, with the aid of insulin, the acidosis has been cleared, which usually takes two or three days at most, I am in the habit of using the Woodyatt diet, generally adopted and proved to clear up acidosis; then, after waiting a little longer, we can tell whether that subject has to use insulin permanently. I think it inadvisable to plunge too precipitately into the use of large doses of insulin. Toxic effects have often been observed in the first few days of treatment when the tolerance has not been known. I rather think it best to put the patient on a rest diet and see what the tolerance is. A few days of waiting—the patient perhaps has had no adequate treatment for diabetes for many years—will not hurt him.

I do not entirely agree with Dr. Rowe in giving the high fat diet. It seems to me that in giving the high increase of calories for the comfort which can be obtained, we do not need necessarily go to the extreme diet, such as advocated by Newberg and Marsh some two years ago. I have yet to see the diabetic that likes to take a high fat diet. I think, therefore, that it is wiser to use a larger dose of insulin, now that it is getting cheaper, and select a diet such as Woodyatt's, which is a very comfortable living diet.

Dr. Walter Timme, New York: One of the important complications in the administration of insulin is the lowering of the blood sugar to a point at which we have a critical low stage, with the possibility of convulsions. A corollary to that is of extreme interest, namely, that certain types of epilepsy—the type that occurs in the early morning with blood pressure and pulse pressure extremely low—if examined closely will be found to have an exceedingly low blood sugar content previous to the epileptic seizure; and from what we have learned of the administration of insulin we are, some of us,

adopting the modes of relief for that type of convulsive seizure in this type of epilepsy, namely, the administration of such things as will provoke stimulation of the sympathetic nervous system, and we give alcohol or coffee, among other things, and glucose. Coffee and alcohol are the two things above all others that heretofore we deprived our epileptics from taking as inducive to attacks; and now the pendulum has swung the other way and we are beginning to get good results, and particularly in epilepsy of this type, by the proper administration of coffee and alcohol.

I should like to have a few moments to discuss Dr. Sansum's statements. We should all like very much to have the active principles of pituitary, parathyroid and the other glands standardized, so that we might know just how much we are using. I wonder whether we are expected to wait until our investigations reach maturity before we use any of the products which now have been put at our command? I do not like the juxtaposition of the terms empirical and haphazard. They do not necessarily belong together at all. You can be haphazard even in a physiological laboratory, curious as it may seem, and I know of a great many empiricists who are quite the other. So I say we should make use of what we have in an empirical way, not haphazard, and determine whether we get results. Whether those results are at all comparative in case after case is a question that may be difficult of solution, of course.

That brings me to the statement made that the only substance that we know of which has an effect upon human economy when given by mouth is thyroxin. That statement was once made at a medical meeting in which very many prominent physiologists were present, and a speaker at that time invited any one of them to take an ounce of adrenalin chloride (1-1000 solution) and swallow it then and there. If it had absolutely no effect there should be no reason for not taking it that way. None accepted the invitation. As a matter of fact, you do not need to experiment on animals or on any other human being than yourself. When you get a chance, take a little adrenalin by mouth and see if you get any effect on yourself, or take a little pituitary substance into a stomach which has no food in it for two or three doses or for two or three days and see whether it has any result upon yourself. You do not need to read a textbook; you do not need to go into the physiological laboratory; you do not need to measure the blood pressure or pulse rate of the animal that has received it. There are certain things our instruments, good as they are, do not measure. There never was an instrument invented that took the place of brains, and so I say that if you think none of these substances is at all assimilable or produces any effect when given by mouth, please try it on yourself.

Parathyroidectomy used to be followed by death with convulsive seizures, and it was thought that this was due to an absence of the parathyroid; later, we found that parathyroidectomized dogs, when given intravenously calcium chloride did not die and they did not get tetanus. Carlson goes further and finds in his laboratory that you can parathyroidectomize animals without giving calcium at all, but simply refrain from giving them a protein diet, keeping them perfectly quiet, and they survive the operation and apparently are none the worse for it.

Dr. J. B. Collip, Edmonton, Canada: It is gratifying to those of us associated in the development of insulin to see, in a little over a year since the first clinical trial was made, that the hormone has been used successfully in the treatment of diabetic patients practically the whole country over and in other countries as well. There is very

little I can add to the remarks which have been made, other than to say that it is quite evident that the speakers have been doing most excellent work in developing insulin therapy.

Very early in my work on insulin I conceived the idea that there would possibly be some fundamental similarity between sugar storage in the form of starch in a plant and sugar storage in the form of glycogen in the animal; between sugar combustion in the animal and sugar combustion in a plant; and because yeast contains sometimes as high as 30 per cent of glycogen, I undertook to apply somewhat the insulin technique to various types of yeast. After about nine months of failure, I prepared an extract from yeast on January 25th of this year, which produced hypoglycemia of a marked degree. The effect did not, however, develop until something like twenty-four hours after the extract was given. I was quite gratified with this result and proceeded to make extracts from various other plant tissue. I first chose a plant which contained no glycogen and no starch, namely, the common onion. I found that extracts from onion tops or roots produced the same effect as yeast, namely, a fall in blood sugar concentration when injected into animals. Now, I should not want to suggest that because one can produce a lowering of blood sugar of normal animals by the injection of plant extracts that these extracts contain insulin, or even an insulin-like substance. I am only prepared at present to say that there is a certain parallelism between the physiological effect of certain plant extracts and certain pancreatic extracts.

Very recently, I have found that the blood of a rabbit in profound hypoglycemia following the injection of a plant extract will produce hypoglycemia in a second rabbit, the blood of a second rabbit will produce a similar effect in a third, and so on, apparently to an unlimited extent. I am not prepared at present to state the possible significance of these observations. Intensive work along these lines will be pursued, however, in order to elucidate this very interesting phenomenon.

Dr. Arthur D. Dunn, Omaha: I wish to emphasize two points already made. First, insulin therapy in its present status does not displace but enhances dietetic therapy. The thorough grounding of the patient in the dietetics of his disease is fundamental and as important as it ever was. It is an unpleasant type of life that must depend for its existence on the daily use of a hypodermic. If the patient's diet can be so adjusted that he can obtain from a balanced diet the requisite number of calories to earn a living without abnormal depreciation of his machine, it is better for him to live without insulin than with. Second, I wish to emphasize the variation of the potency of insulin in our experience. Recently we have had a patient who received 45 units of insulin daily to absorb a spill of 30 grams of glucose daily.

The use of insulin in our limited experience in surgical interventions has been of extreme value. By the use of insulin it seems we can do with impunity certain things we could not do before. One interesting experience was with an obese subject with a rather mild type of diabetes. This patient weighed 240 pounds; he had a total glucose tolerance of about 140 grams. Prostatectomy was performed; the operation was difficult, and was followed in twenty-four hours by symptoms of acute dilatation of the stomach. A stomach tube was passed, although the distention was little, and a hemorrhagic fluid was obtained from the stomach. I am certain that this man did not have an ulcer. Now, during the following five days no food could be taken. If 800 cc. of fluid were ingested during twelve hours he would

give back through the stomach tube anywhere from 1000 to 1200 cc. There was little fluid passing the pylorus. At the end of five days his urinary glucose output per diem was 13 grams; his blood sugar was 320 milligrams per 100 cc. At this time he was put on 80 grams of glucose with 40 units of insulin; at the end of the sixth day he desugarized with a blood sugar of 160 milligrams. I feel that the insulin was of crucial importance in the handling of this case.

Dr. A. L. Walters, Eli Lilly & Co., Indianapolis: I have been associated in the commercial manufacture ofletin or insulin during the past year, and I think it is incumbent on me to answer Dr. Sansum's question regarding the standardization of the unit. The original unit was the amount of insulin required to lower the blood sugar of a 2 kilogram rabbit to a point where the rabbit showed convulsions. At that early stage it was thought that such a unit would be too large for clinical application and it was therefore decided that a smaller unit should be adopted which was defined as the amount which would lower the blood sugar of a 1 kilogram rabbit to .045 per cent of sugar and produce convulsions. Working with a large number of rabbits, however, it was soon found that 1 kilogram rabbits did not give as constant results as the heavier animals. Therefore, we began using the larger animals, so that the standard rabbit used at the present time weighs in the neighborhood of 2 kilograms.

Contrary to what Dr. Sansum has found, the convulsive dose does not vary in direct proportion to the weight. It does vary as the square of the weight almost mathematically, as shown by a very large series of tests. A 2 kilogram rabbit will require four times as much as a 1 kilogram rabbit. The very early pancreatic extracts made were not stable. That was one of the problems that had to be solved—to make a preparation that would be stable. Therefore, in the earlier preparations to compensate for loss by deterioration, a slight excess was added over the amount stated on the label, so one unit was really a little stronger than its definition would indicate. When it became time to put this preparation generally on the market, the whole subject was gone over and the definition now adopted does not in any way change the strength of the preparation; and the present unit is defined as one-third the amount required to produce lowering in blood sugar of a 2 kilogram rabbit to the convulsive stage. The strength has not been changed.

Each batch is tested and it is tested on not less than one hundred rabbits, and sometimes four or five hundred, and subsequently each lot is tested in at least six different clinics, and sometimes eleven. These clinics report back their clinical tests and we feel that the strength of the preparation does not vary more than other products tested biologically.

Dr. O. M. Gilbert, Boulder: There is one other field that seems to be opened up in this respect and that is the utilization of glucose intravenously. In the present conditions we are now fearful of it. That comes strongly to my mind from recollection of a patient treated within the past year, a case of nephritis in which the vomiting was so persistent that we were able to sustain the subject only by the intravenous use of glucose. Upon administration of 500 cc. of 15 per cent solution, 75 grams of glucose, there was no glycosuria and no elevation of the blood sugar, but we found that with 600 cc., to which we tried to increase it, the sugar overflow occurred in the urine and rose to 0.2 in the blood. We were able to sustain his subject for some little time, until he developed a convulsion.

to sugar—he began constantly to excrete sugar, and finally upon the cessation of the intravenous use of glucose he continued to excrete sugar for four days. This meant to us, of course, that his islands of Langerhans had been stimulated and overworked until they had, so to speak, taken on the habit of “working overtime” and went on doing it.

It appears to me that with the use of insulin so the man could have metabolized that sugar, which was perhaps aggravating his kidney condition, we might have tided him through.

Dr. Wm. Engelbach, St. Louis: We are frequently told that organotherapy is more or less empirical and given in most cases without result. I take it for granted that reference is made to results observed by the physiologist upon animals in the laboratory. But even in clinical circles there is great difference of opinion and contention with regard to the effects of ductless gland therapy. I think that results depend greatly upon a number of factors that we have not quite appreciated.

In the first place, in addition to the *questionable potency* of the various products used, there is no doubt that we are making diagnoses entirely too late in a great many ductless gland disorders to obtain good results. We begin to treat cases six to ten years after a gland has been out of function and expect results from the administration of a known hormone. Then, second, I feel sure from our own personal experience that our diagnoses have been incomplete. I know we have treated pluriglandular diseases for uniglandular disorders; for instance, treating a thyro-pituitary syndrome for a simple hypothyroidism, giving thyroid instead of thyro-pituitary substitution therapy. And, third, I believe that we are not treating subjects at the most opportune age. There are certain ages in glandular disorders at which time, if treatment is instituted, favorable reactions are produced; whereas, if the same patient or the same disorder is treated at another age, the treatment is of little avail. For instance, hypogonadism, when treated just before the stage of maturity, offers very much better results than when treated at the age of twenty-five.

As a general rule, those who have considerable experience with the use of these glandular preparations are not over-enthusiastic about the oral administration of a great many of them. We must also admit that the older the subject and the more glands there are involved in one syndrome, the less likely we are to get results with any sort of treatment. Another source of poor results can be traced to mistakes in diagnosis, illustrated in the treatment of amenorrhea or dysmenorrhea. If we are able to make a proper diagnosis of the cause of amenorrhea or dysmenorrhea, better response to treatment will occur. Corpus luteum, so commonly employed, will not cure menstrual disorders due to thyroid or pituitary deficiency.

There are many definite positive observations in the clinical study of the human endocrine organs that I believe the laboratory cannot duplicate in animal experimentation. They are making experiments on a group of animals concerning whose ductless gland function comparatively little is known. They are not sure that they are not dealing with hyperpituitarism or hypergonadism in certain animals at a certain age, which estimation I believe can be made in the human being by the clinician. Again, there are some measurable results in the human subjects which cannot ever be estimated in animals; for instance, the change in adiposity as the removal of the girdle adiposity with pituitrin. The effects upon the mental, menstrual, and osseous development and function are other striking examples. A careful roentgen estimation of osseous development at various ages

proves that all these glands have decided influence upon the skeletal growth. The latter is demonstrated by the effect of ductless gland treatment upon the appearance of the nuclei of certain bones and the fusion of epiphyses in positive endocrine disorders. I believe that these clinical observations are just as scientific, exact, and convincing as the experiments of the physiologist. What we need is more discriminating, discerning clinical studies along the line of the positive therapeutic effects of these interesting disorders of the internal secretions.

Dr. A. H. Rowe, Oakland, Calif.: I feel that we are very fortunate to have had a word from Dr. Collip today. We all know what a definite part he has played in the development of the insulin problem, and I think also that we are privileged to have had a word from Dr. Walters, because without question on his effort has depended a great deal the efficiency of the development of the problem and the manufacture of insulin by Eli Lilly & Co.

I chose definitely to include the word "complications" in my topic today because I feel that it is not only in the treatment of severe cases that were heretofore unable to be controlled satisfactorily without insulin that insulin has such a remarkable effect, but it is also in cases such as Dr. Dunn has spoken of today, severe surgical complications and severe infections that have been the great problem and bugbear of diabetics heretofore, that insulin is going to be of great service in the future.

Dr. W. D. Sansum, Santa Barbara: It took nearly forty years to develop a pancreatic extract and I feel that we should get further if we would put more effort into the laboratory animal than we are doing. It certainly is agreed that at certain times you get results which are good from these various pancreatic products.

About a year ago I, with two other residents of my own town, went to Los Angeles. We worked all day on the floors ourselves to get the glands fresh; we took out sixteen hundred glands from beef, sheep and calves very carefully, put them in alcohol, transported them back to Santa Barbara, and from those sixteen hundred glands we got a good grade of water. Many times during the summer we got a good grade of water, and when we administered this to patients it was of no value.

With respect to regeneration—and we have given a good deal of thought and attention to that—we had under our care many carefully measured patients in whom we could say the tolerance of this one is 50, 60, 70, etc. They had what we considered good care; they had been kept free from blood sugar and kept nourished by keeping them in bed. In those patients we have not observed very material growths in tolerance. A patient of 50 may have developed a tolerance of 60. A patient who had been mismanaged might come in loaded with acidosis and sugar; in many of those subjects we have found a marked growth of tolerance, and we believe that the pancreas can get over its fatigue; but whether any regeneration will take place we have not any evidence as yet.

The high fat diet we never use unless the patient is gaining weight. We do in some instances give five hundred calories of fat in addition to the Woodyatt diet, but we do not do that unless the patient is constantly gaining weight at a rate which exceeds the amount of fat we are giving.

Dr. Dunn may have got hold of some insulin which was not quite as strong as it should be. We have had batches of our own and others which have been worth 0.6 of a gram per cc. Six-tenths of

a gram at 30 would require, of course, 50 units, so that is nothing out of the ordinary.

I rather suspect that in a subject with postoperative acidosis, there is sometimes suppression of many of the internal secretions, and perhaps a little insulin might be a good thing.

The method which Dr. Collip has devised in the beginning is a method of extracting insulin which has stood the test of time, and that is a very important thing to say about a method which is devised as rapidly as he was able to devise that method.

THE INCIDENCE OF ENDOCRINOPATHIES IN THE PUGET SOUND BASIN

A PRELIMINARY REPORT

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This paper is presented in the hope that it may arouse interest both in the study of the geographical distribution of endocrinopathies and in the establishment of prophylaxis in the treatment of simple goiter in the Northwest.

GOITER

From time to time, comments have appeared in the literature relative to the frequency of goiter in the Northwest. However, it was not until the results of the draft examination were reported that statistical information of value was available. The results of that examination at once forced the acceptance by the Northwest of the unenviable position of priority in the incidence of goiter in the United States.

In the War Department publication, *Defects Found in Drafted Men* (1), which gives an analysis of about one-half million men rejected by the medical examiners of local boards, and of two lots of about a million each who were examined at mobilization camps during the physical examinations of the draft in 1917-18, Idaho is shown as having the highest incidence of simple goiter, a ratio of 26.91 per thousand men. Oregon is second on the list with a ratio of 26.31 per thousand men. The ratio for Washington is 23.4 and for California but 4.45, or a ratio practically the same as that for the entire United States, *i. e.*, 4.35 (Table 1.).

Exophthalmic goiter, according to the aforementioned publication, is most prevalent in the State of Washington. The ratios per thousand men for Washington, Oregon and California are 9.42, 6.37 and 1.95, respectively (Table 1.).

In sharp contrast to the figures just considered are those of Kerr (2), who, while stationed at Camp Lewis, examined

21,182 recruits for goiter. According to this author, goiter occurred in 21.0 per cent of the entire number of men examined. Goiter was found in 39.0 per cent of the Washington men, 32.0 per cent of the Oregon men, and only 8 per cent of the California men (Table II). Kerr's data are of further interest in that he reports the distribution of goiter in the families of the 4,693 goiterous recruits as follows: Sisters 52.0 per cent, mothers 29.0 per cent, brothers 16.0 per cent and fathers 3.0 per cent.

The wide differences in the ratio of goiter between the figures of the War Department and those of Kerr are incongruous; however, I am led to believe that the figures of the latter are more nearly representative of the condition as it exists.

TABLE I. NUMBER OF CASES OF ENDOCRINE DISTURBANCES FOUND IN APPROXIMATELY TWO AND ONE-HALF MILLION DRAFTED MEN

		WASHINGTON		OREGON		CALIFORNIA		U. S.	
		No.	Ratio	No.	Ratio	No.	Ratio	No.	Ratio
I.	Thyroid								
	a. Goiter								
	1. Simple	832	23.40	421	26.31	359	4.45	11,971	4.35
	2. Exophthalmic	335	9.42	102	6.37	157	1.95	8,647	3.14
	b. Cretinism and Myxedema							67	-
II.	Diabetes Mellitus	9	0.25	11	0.69	31	0.38	740	0.27
III.	Anorchism, Monorchism, Cryptorchism and Hypospadias	137	3.85	57	3.55	284	3.53	8,538	3.10
IV.	Gigantism							7	
V.	Acromegaly							48	
VI.	Addison's Disease							14	
TOTAL		1,313		591		831		30,032	

Data obtained from Defects Found in Drafted Men, 1920, War Department, Office of the Surgeon General.

A third series of statistics of a reliable nature relative to the incidence of goiter in the Northwest has been compiled by Hall (3), of the University of Washington.

According to the data of this observer, the percentage of goiter for the State of Washington is 26.37. An examination of over 13,000 students of the University of Washington from 1908 to 1921 shows that 21.5 per cent of the men and 33.2 per cent of the women are goiterous. The percentages of goiter among the students from without the State are as follows: Alaska 19.0, British Columbia 24.0, Oregon 17.0 and Idaho 28.0.

The appearance of goiter is strikingly irregular for the various counties of the State of Washington. However, those counties of the mountain slopes have a consistently higher percentage. It appears that the counties of the eastern slope of the Cascade Mountains are most severely affected with goiter;

however, the highest percentage for any one county was found in Clallam County, which is located along the shores of the Strait of Juan De Fuca. For the details concerning the distribution of goiter by counties see Figure 1.

Hall, in a letter to Dr. V. C. Vaughn, dated Oct. 29, 1921, concerning the goiter situation in and about Seattle, states: "I have experienced great difficulty in carrying out the researches that I wished on account of the antagonism of the Christian Scientists. We have had much trouble here, and recently the school board passed an ordinance prohibiting anyone to carry on any style of medical research in the schools unless it be granted by a city or state ordinance. This was brought about as the result of the work I was doing in the public schools with the

TABLE II. GOITER IN RECRUITS EXAMINED AT CAMP LEWIS, WASHINGTON

I. Distribution of goiter in recruits from the Pacific Coast States.				
State	No. Recruits	No. Cases	Per Cent	Ratio per 1000
Washington	2,114	826	39.0	390.00
Oregon	923	291	32.0	320.00
California	4,364	360	8.0	80.00
GRAND TOTAL...	21,182	4,693	21.0	210.00
II. Classification of the 4,693 cases of goiter.				
1. Moderately large or large..	1,276		27.0	270.00
2. Small	3,417		73.0	730.00
III. Distribution of goiter in the families of the 4,693 recruits with goiter.				
1. Sisters	554		52.0	520.00
2. Mothers	311		29.0	290.00
3. Brothers	172		16.0	160.00
4. Fathers	33		3.0	30.00
IV. Disturbances associated with goiter.				
1. Hand tremor.....	2,591		55.0	550.00
2. Moist, blue hands.....	4,123		88.0	880.00
3. Curved finger nails.....	2,612		56.0	560.00

Table compiled from data gathered by Dr. W. J. Kerr, Arch. Int. Med. (Chicago), 1919, 24, 347-358.

sanction of the medical director and superintendent of public instruction. I managed to survey eight schools before the pressure was sufficient to have me stopped. Starting with the kindergarten in the schools, I examined every boy and girl"—A sad commentary on those who boast of their state, climate and low mortality rate. But why quarrel with those who oppose us when in our own midst are those who, like a physician and surgeon of good standing, advised an inquiring mother to spank

her little daughter if she again showed anxiety concerning her goiter.

The grade school examination referred to by Hall in the preceding paragraph, showed goiter to be present in 41.5 per cent of the boys and 47.7 per cent of the girls between the ages of 6 and 14 years. As mentioned by Hall, "the percentages of goiter in these children are roughly the same for both boys and girls until the twelfth year is reached, when the girls shoot way ahead of the boys, the boys not approaching them until a few

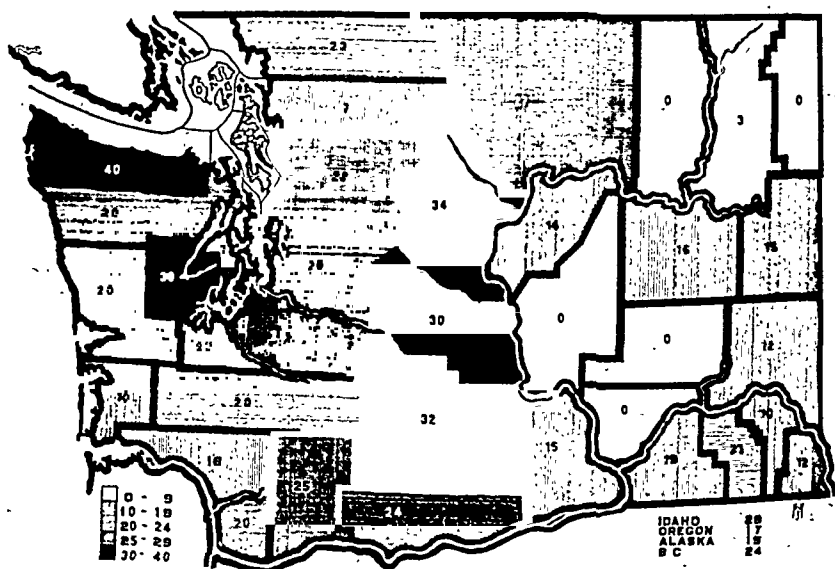


Fig. 1, Distribution of Goiter in Washington by Counties.

years later." For further details concerning the grade school children see Table III and Figure 2.

Goiter was observed by Hall in the students of one high school in 38.3 per cent of 575 boys and 65.6 per cent of 521 girls (Fig. 2).

"Fat boys and girls had no thyroid that could be palpated or observed, although this was not on account of the fat. It was also interesting to note that in a class of defectives only four thyroids could be palpated out of a class of thirty, *i. e.*, 13 per cent." This statement is of considerable personal interest, for I have been repeatedly impressed with the infrequency of palpable thyroids in obese and mentally defective children, although, at present, I have no figures on this point.

According to the draft examinations tachycardia occurred in Washington recruits in a ratio of 7.65 per thousand men. The ratio for the United States was 4.45. In discussing this point the conclusion is reached "that the relation of tachycardia

TABLE III. INCIDENCE OF GOITER IN THE SCHOOLS OF SEATTLE

GRADE SCHOOLS			ONE HIGH SCHOOL				
Age	Boys	Girls	Age	No. Exam.	Per Cent	No Exam	Per Cent
	Per Cent	Per Cent					
6	21.0	25.4	14	96	42.7
7	35.5	33.5	15	165	47.3	176	66.5
8	38.7	36.4	16	151	30.5	161	60.3
9	35.0	43.0	17	97	33.0	105	64.8
10	36.0	48.0	18	66	37.9	79	70.9
11	42.4	45.0	STUDENTS UNIVERSITY OF WASHINGTON				
12	47.0	57.7	No. examined was over 13,000.				
13	49.0	70.0	Men				21.50
14	60.0	70.0	Women				33.20
			General Average of State.....				26.37
Average 41.5			Total 575		38.3	521	65.6

Table compiled from data gathered by Dr. David C. Hall, Professor of Hygiene, University of Washington, Seattle.

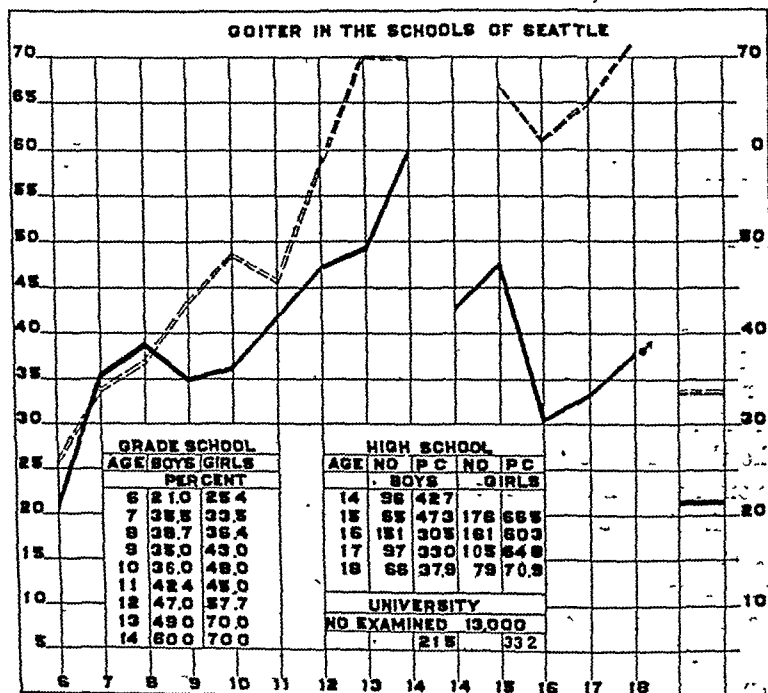


Fig. 2, Goiter in Schools of Seattle

and exophthalmic goiter is fairly close, but that tachycardia is more widely spread throughout the population than exophthalmic goiter." According to Kerr, hand tremor occurred in 55 per cent of the 4,693 goiterous recruits examined at Camp Lewis; moist, blue hands occurred in 88 per cent, and curved finger nails in 56 per cent of the recruits.

The presence of goiter was recorded in only 167 of 3,254 consecutive clinical cases passing through our own offices (Table IV). This low figure, 5.1 per cent, in no way represents the incidence of goiter among Seattle patients for the very simple reason that a systematic search for goiter was not made. Possibly the existence of goiter is taken for granted and mention not made of it unless symptoms referable to the gland are manifest. To quote a colleague on this point: "Goiter is so common that we pay no attention to it"—really a better frame of mind than that of carrying animosity towards those who are sufficiently interested in their condition to seek the advice of a physician. The figures, while interesting, should not be taken as representative; they are the results of six examiners and represent, in the majority of instances, cases only sufficiently manifest to attract notice.

The degree of clinical attention demanded because of thyroidal disturbances in and about Seattle is indicated by the records of one hospital in which surgery was performed in 300 or 4.2 per cent of 7,000 consecutive surgical cases.

SEX

Defects of the sex organs were recorded in 8,538 of the approximately two and one-half million men examined by the Draft Board (Table 1). The defects included anorchism, monorchism, cryptorchism and hypospadias. As shown in Table 1, the three Pacific Coast States have a higher incidence of such anomalies than the ratio for the entire United States.

In the 202 endocrinopathies of our own clinic but one case of eunuchoidism, and one of surgical castration of the female were recorded. A tentative diagnosis of vicarious menstruation was made in one case (C. 2118). This diagnosis was made, and that with hesitancy, because of the spitting of bright blood a few hours previous and during the early part of each menstrual cycle, over a period of about seven years. The establishment of

pregnancy in this case was followed by complete cessation of both the menstrual and oral flow.

PANCREAS

Diabetes mellitus was found in 10, or 0.32 per cent of the 3,254 patients passing through our clinic. This figure is decidedly larger than that recorded for drafted men, *i. e.*, a ratio of 0.27 per 1,000 men. Diabetes occurred in a ratio of 0.25 per thousand recruits in the State of Washington, 0.69 in Oregon and 0.38 in California (Table 1).

PITUITARY

Acromegaly was found in only 48, and gigantism in 7 of the total number of men examined for the Draft (Table 1). Endocrine disturbances primarily referable to the pituitary

TABLE IV. INCIDENCE OF ENDOCRINOPATHIES AS OBSERVED IN 3,254 CONSECUTIVE CLINICAL CASES (POLYCLINIC, SEATTLE)

<i>Disturbance</i>	<i>Number</i>	<i>Per Cent</i>
A. Thyroid		
1. Goiter	167	5.10
2. Cretinic	8	
B. Pancreas		
1. Diabetes mellitus.....	10	
C. Pituitary		
1. Froehlich's syndrome.....	6	
2. Gigantism	3	
3. Infantilism	1	
4. Diabetes insipidus.....	1	
D. Gonads		
1. Male		
a. Eunucoidism	2	
2. Female		
a. Castrate	1	
b. Vicarious menstruation (Case C 2118)	1	
E. Thymus		
1. Status thymolymphaticus.....	2	
TOTAL.....	202	6.21

gland appeared in 9 of our cases as follows: Froehlich's syndrome, 6; gigantism, 3; infantilism, 1, and diabetes insipidus, 1 (Table IV).

SUPRARENALS AND THYMUS

Addison's disease was found in 14 of the two and one-half million men examined for war services. This disease was not observed in the 3,254 cases of our clinic.

Status thymolymphaticus occurred in 2 of the 202 cases of endocrine disturbance of our own series. In one patient, a girl

according to Plummer's practice. It rather emphasizes the necessity for accurate diagnosis as pointed out by Dr. Boothby.

Dr. Else appears to have misunderstood Dr. Boothby. The latter said distinctly that in toxic goiter cases iodine is harmful—as all of us know—and he conceded that iodine might perhaps be harmful in certain cases of adenoma without toxic symptoms, if it awakened a latent toxic tendency. But in Graves' syndrome there is a different condition. In this iodine is employed to prevent the post-operative collapse sometimes observed, and is given on certain definite indications, the chief of which is the basal metabolic rate. If I apprehend the reasoning correctly, it is that in one set of cases there is a quantitative change, namely excess of normal secretion, therefore an excess of iodine, or perhaps an excessive supply of iodine in the secretion as well. In the other case—Graves's syndrome—there is a perverted secretion, and upon the possibility that this perversion may be loss of iodine, Dr. Plummer and his associates are working out a scientific method of discrimination. Whether this theory is correct, further study is required to show; but meanwhile we have the very practical results reported, which do mark a distinct advance in both medical and surgical handling of Graves's syndrome. With sufficient individualization of patients, the method should be applied by all of us who have the opportunity, so that its indications and limitations may be clearly established.

Dr. Homer Wheelon, Seattle: We have a very serious condition in the State of Washington in goiter, a very high incidence. We are not permitted at the present time to carry on examinations in the schools, and our information must be gathered haphazard from various sundry sources.

Dr. Else, in his statement concerning the administration of iodine, is, to my mind, entirely correct. Very disastrous and undesirable results have been obtained by giving iodine to a certain number of patients, and I do not believe that prophylaxis should be a promiscuous affair. We have all grades of goiter, and some of them, while apparently simple when thoroughly worked out, are not so simple.

My own hope is to arouse enough interest that we may be at least permitted to do something in the treatment of goiter in the Pacific Northwest. I am delighted to know that Dr. Else and his co-workers are carrying on a similar work in Oregon.

ONE RELATION OF GLYCOSURIA TO KIDNEY PERMEABILITY

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The presence of sugar in the urine per se is not sufficient proof that one is a diabetic. Many normal persons show glycosuria without fasting hyperglycemia, the sugar in the urine in such a case indicating merely that the renal filter is permeable to a low blood sugar content. Thus in a series of 714 observations, 13.8 per cent showed glycosuria in the presence of normal blood sugar content.*

On the other hand, an inverse relation is sometimes found, viz., aglycosuria in the presence of hyperglycemia. In fact, this is quite a common condition, for, while in the early stages of diabetes the kidneys may be permeable to sugar at a blood sugar level of between 160-180 mg./100 cc., after the hyperglycemia has persisted for several years the kidney will not be permeable until the blood sugar content is above 200 mg./100 cc. It follows that one can only venture a guess as to the diabetic status of an individual from the result of an examination of the urine. The true condition can be determined only by a blood sugar estimation, made after a sufficient period of fasting, for a postprandial sugar content gives no information within a period of at least three hours after the meal.

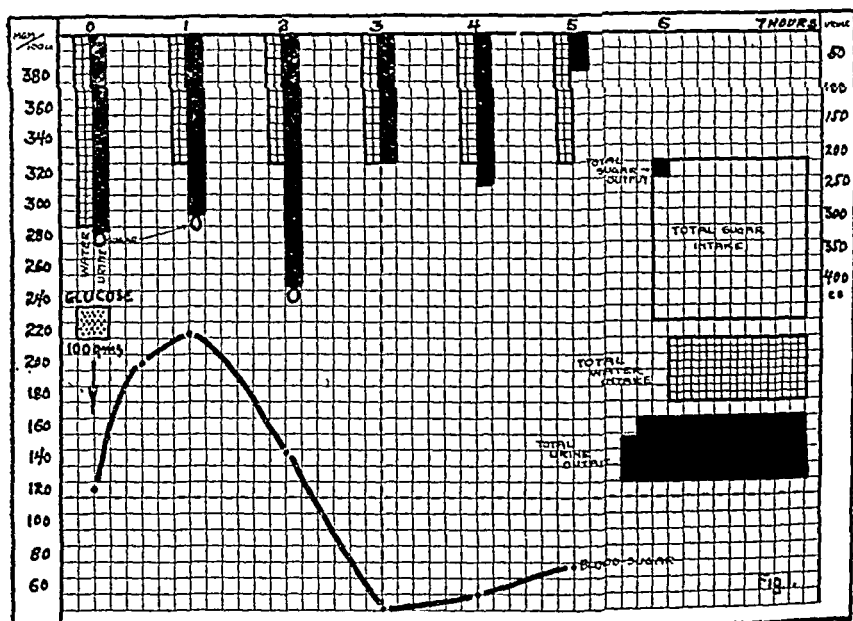
Let us suppose, for example, that the kidneys of each of two patients are permeable to sugar at a blood sugar level of 140 mg./100 cc. and of 240 mg./100 cc., respectively. Since the blood sugar of anyone, whether diabetic or not, can be brought to a normal level by a selected diet, let us suppose that the blood sugar content of each of these patients is normal, that to each patient, 50 gm. of glucose is given by mouth on a fasting stomach, raising the blood sugar in each case to 200 mg./100 cc., and that the hourly blood sugar estimations on these subjects

* Glucose tolerance and its value in diagnosis, John (H. J.), J. Metab. Research, 1922, I, 497-548.

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show that the first is not a diabetic, while the second is a diabetic.

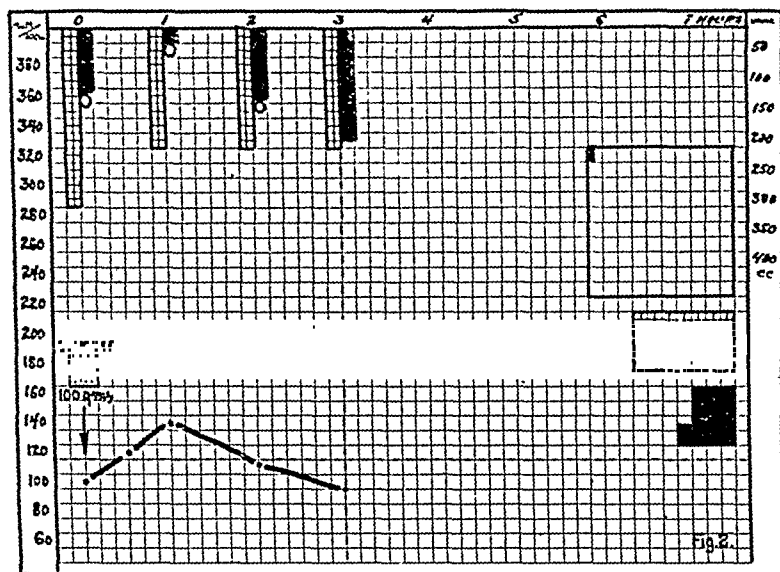
The hourly urine examinations in the first case will show that glycosuria appears when the blood sugar reaches about 140 mg./100 cc. and persists as long as the blood sugar stays at or above that level, while in the second case we shall find that no sugar appears in the urine at any time, for although the blood sugar rises to 200 mg./100 cc., it does not reach the threshold of kidney permeability for glucose. In the presence of high hyperglycemia, therefore, we fail to find glycosuria,



even though the blood sugar curve shows that this subject is a diabetic.

Such cases as these, *i. e.*, glycosuria in a non-diabetic and aglycosuria in a diabetic, are of frequent occurrence and they indicate the essential need of checking the urinary findings by accurate blood sugar determinations before forming a final judgment as to the diabetic status of the patient. A case which I reported a year ago illustrates this point, and it seems well at this time to review briefly several other cases of this type in order to emphasize a problem that the physician meets in his daily practice, to point a way toward its solution, and to interpret the laboratory findings in each case.

Case No. 1: A married woman, 66 years of age, came to the clinic complaining of rheumatism. The family history was negative. She had had grippe and rheumatism and sciatica 6 weeks before this consultation. For the last 8 months she had had frequency of urination but no loss of weight and no thirst. She had always been fond of sweets and had eaten them freely. The routine examination showed sugar in the urine. Examination of the blood showed in mg./100 cc., blood sugar, 113; urea, 22.9; chlorides, 574. A glucose tolerance test was made with the findings given in the table and graphically shown in Chart I, which demonstrate that this is a case of glycosuria in a non-diabetic subject.

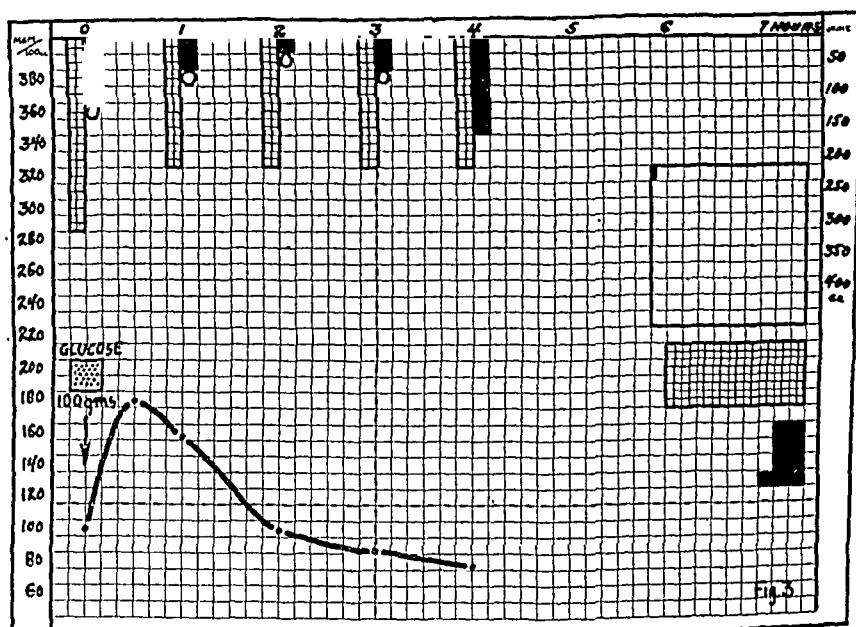


Case No. 2: A single woman, aged 22 years, came for a consultation because of increasing weight, having gained 20 pounds during the preceding 2 months. Her family history was negative. She had had diphtheria, scarlet fever, pneumonia, grippe and tonsillitis; she complained of a "weak spell" every afternoon when things became blurry before her eyes, of feeling "dopy" and of sleeping a great deal. During the preceding 6 months she had had dribbling of the urine, but at the time of consultation thought she was passing more urine. She suffered from occipital headaches, and a coarse tremor of the hands. The Wassermann test was negative, spinal fluid negative, x-ray of sella turcica negative. The result of the glucose tolerance test is shown in the table and in Chart II.

Joslin and others have called attention to the importance of watching for diabetes in fat people. Whenever I see a middle aged fat patient, I always wonder whether the adiposity betokens a beginning diabetes or whether it is merely a normal process. When in addition to the increasing weight there is some sugar in the urine, the necessity for a glucose tolerance

test is clearly indicated as the only means by which the true status of the subject can be determined. In this case, in spite of the sudden adiposity, there was no decrease in the carbohydrate metabolism, and the glycosuria therefore was of no significance as it indicated merely a permeable renal filter.

Case No. 3: A physician, 37 years of age, submitted himself to examination simply for the value of the data which might be obtained. He was in perfect health; he had had measles, malaria, carbuncles and influenza; there was no familial diabetic history. The physical examination was negative; the Wassermann test was negative; a glucose tolerance test gave the findings shown in the table and in Chart III.

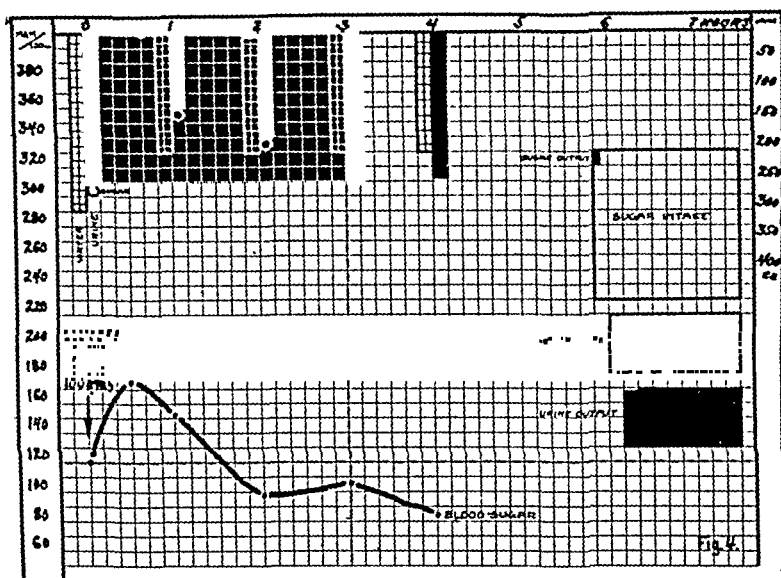


In a perfectly normal subject the glycosuria had no significance as the laboratory findings disclosed an increased permeability of the renal filter for glucose with a normal carbohydrate tolerance.

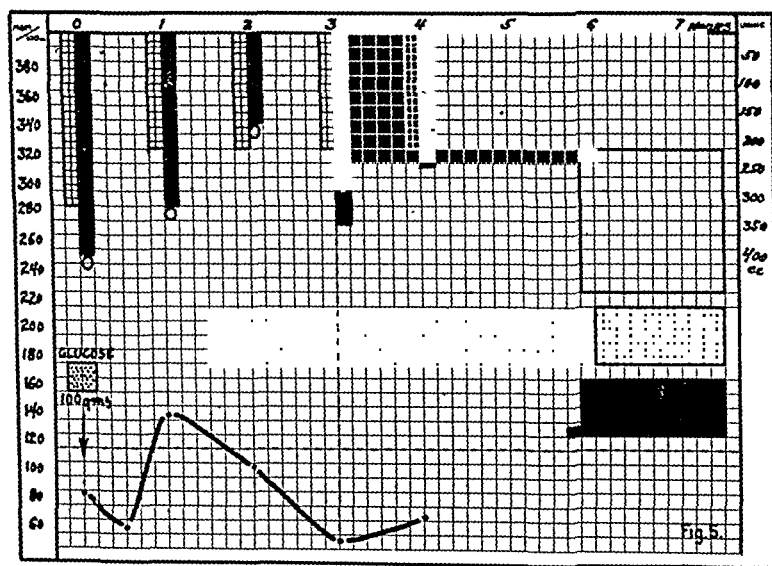
Case No. 4: A young single woman, 17 years of age, complained of nervousness and a slight cough. The family history was negative. The patient had had tonsillitis, grippe, malaria, tonsillectomy, adenoidectomy and herniotomy. She had noticed a slight enlargement of the thyroid gland at puberty. She had experienced no loss of weight nor strength. The Wassermann test was negative; blood chemistry examination showed sugar 120, urea 15.7, chlorides 587 mg./100 cc. Sugar was found in the urine. The results of a glucose tolerance test are given in the table and in Chart IV.

The glycosuria in this case betokened only an increased

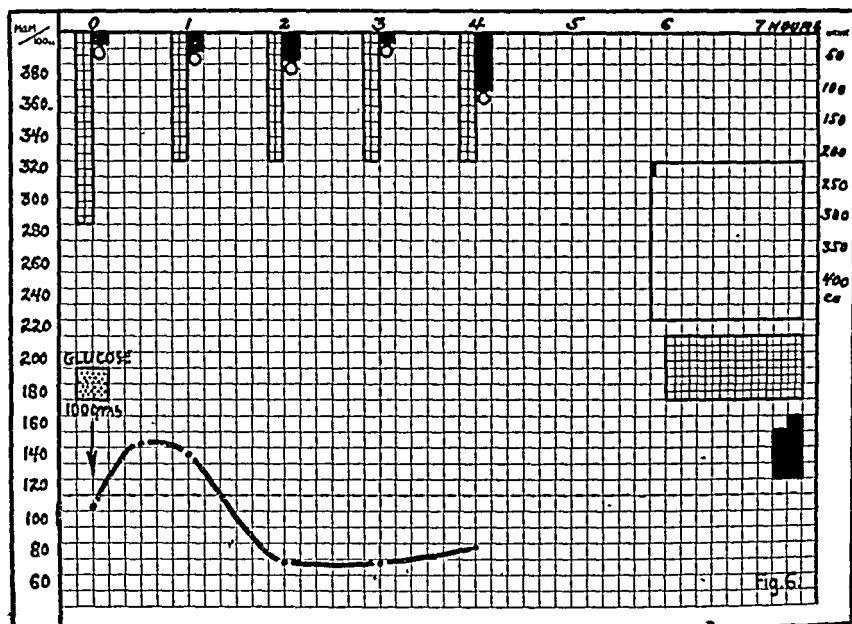
renal permeability to sugar in a mild case of hyperthyroidism, the carbohydrate tolerance being normal.



Case No. 5: A married woman, 40 years of age, came in because of headaches. Her brother had diabetes. She had 4 living and well



children and had had a number of miscarriages. She had had pneumonia, grippe, tonsillitis and rheumatism. Physical examination was negative; the Wassermann test was negative; the blood pressure was 130/70. Routine examination of the urine showed sugar. A glucose tolerance test gave the findings shown in the table and in Chart V.

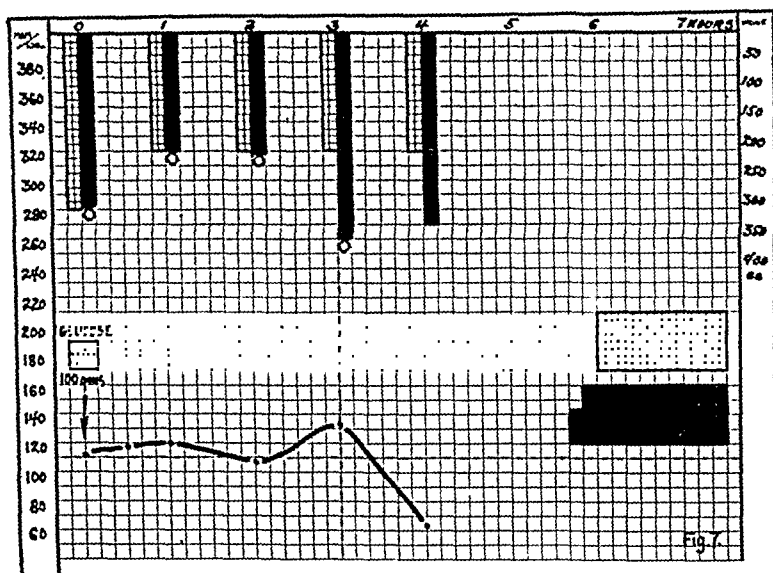


In a middle aged woman with a familial recurrence of diabetes, the presence of glycosuria was bound to excite suspicion. Here again, however, the laboratory test revealed an unimpaired carbohydrate tolerance, showing that the sugar in the urine was due to an increased renal permeability.

Case No. 6: A married man, 34 years of age, came in because on the preceding day life insurance had been refused him on account of glycosuria. His father and a paternal uncle had died of diabetes and a brother had a severe case of diabetes. The patient had been married for 11 years and had 3 living and well children. He had had typhoid fever, grippe and gonorrhea, but during recent years had been in perfect health. His physical examination was negative: the Wassermann test was negative; sugar was present in the urine; blood urea, 14.4; chlorides, 490 mg./100 cc. The glucose tolerance findings are shown in the table and in Chart VI.

With such a familial history of diabetes it was certainly natural for the man to feel certain that he had diabetes when sugar was found in his urine and life insurance was refused. The glucose tolerance test showed, however, that he was not a diabetic but a perfectly well man, with only a renal filter permeable to glucose at a low blood sugar level. This man has been well and hard at work ever since.

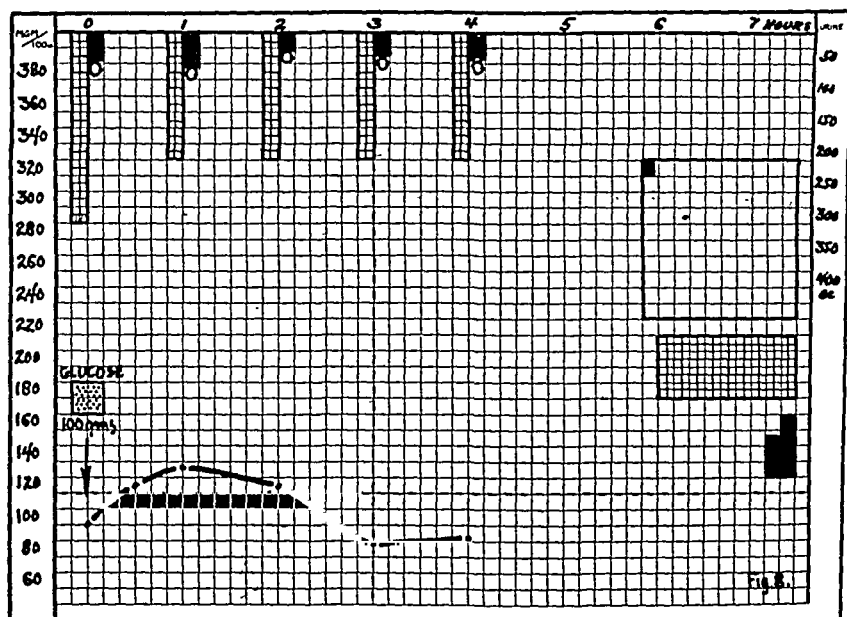
Case No. 7: A single man, 22 years of age, complained of indigestion. His family history was negative. He had had typhoid fever at the age of 2 years, influenza 4 years ago and tonsillitis since the latter date. He had been refused insurance on account of the presence of sugar in the urine and for 2 years was treated as a diabetic by his physician. Physical examination was negative except for a slight tenderness below the umbilicus. A glucose tolerance test showed the findings given in the table and shown in Chart VII.



This man had a low renal threshold for glucose which accounted for the glycosuria, but had no relation to his ability to utilize carbohydrates, which was excellent. Without the information gained from the glucose tolerance test this man might have continued to be treated for diabetes and would inevitably have suffered continually and unnecessarily from his depression of spirit and increased bodily weakness as the result of his limited diet.

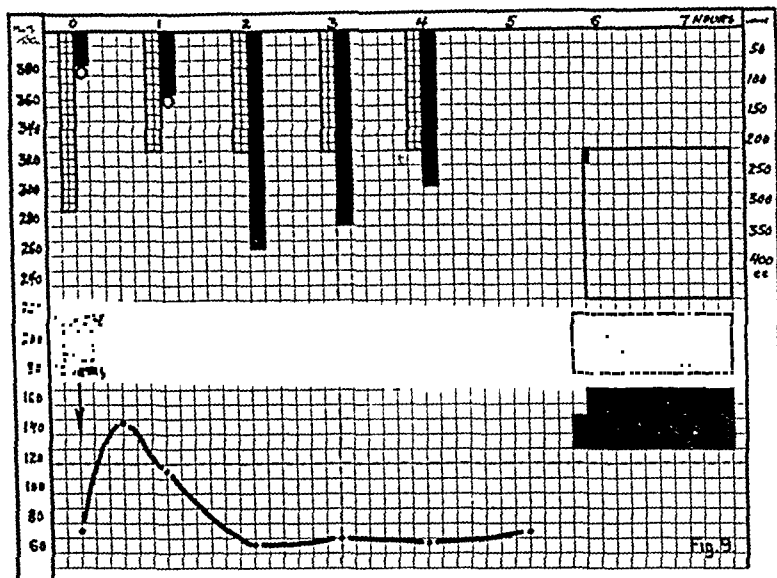
Case No. 8: A physician, 44 years of age, came in because of sugar in the urine. His father had died of diabetes and the discovery of glycosuria in himself had frightened and depressed him. He had been married 13 years and had 2 living and well children. At the age of 9 he had had measles followed by a cough. He had fibrosis of both apices of the lungs but no acid fast bacilli were found in the sputum. Otherwise the physical examination was negative. His best weight had been 130 lbs., but his weight then was 112 lbs. The Wassermann test was negative; blood sugar, 100 mg./100 cc.; plasma chlorides, 575 mg./100 cc.; urea, 35 mg./100 cc. A glucose tolerance test gave the findings given in the table and in Chart VIII.

As in the preceding case the familial diabetic history and the finding of glycosuria naturally aroused an extreme apprehension of diabetes. Again in this case the glucose tolerance test showed the glycosuria to be due entirely to a very low renal threshold. The good carbohydrate tolerance ruled out diabetes.

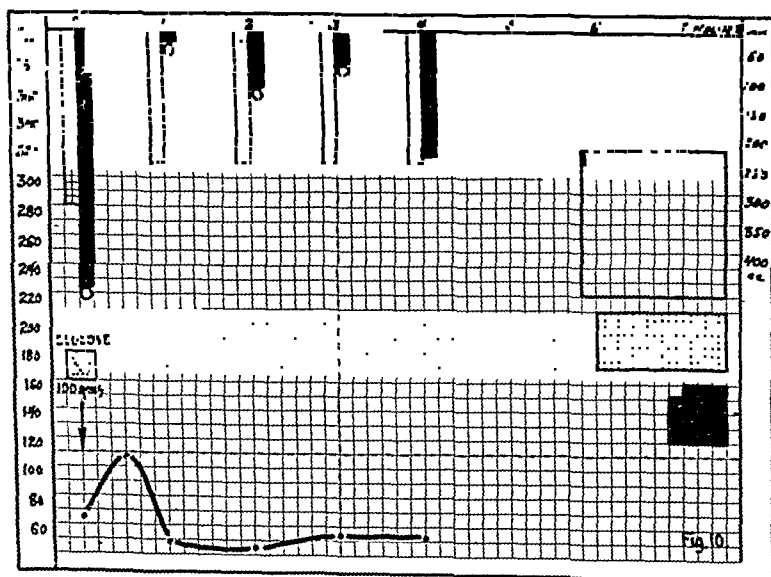


Case No. 9: A single man, 22 years of age, came in because of infantilism and weakness. His family history was negative. He had had no childhood diseases; he had had influenza 2 years before. He was born in Russian Poland, at full term. When he was about 15 months old, his parents first noticed that he was not normal. He did not get along well in school. He had a high, squeaky voice and his ideas were childish. An x-ray examination of the sella turcica was negative; basal metabolism, -17 ; Wassermann, negative; blood sugar, 84 mg./100 cc.; urea, 14.1; creatinin, 1.08 mg./100 cc.; chlorides, 573 mg./100 cc. A glucose tolerance test was made with the results given in the table and in Chart IX.

The glucose tolerance curve was typical of hypopituitary disease associated with a very low renal threshold for sugar, which, however, is not always associated with hypopituitarism. Such a patient could be starved almost to death and would still show sugar in the urine. The glucose tolerance test ruled out diabetes and confirmed the familiar observation that hypopituitary disease is associated with an increased carbohydrate tolerance.



Case No. 10: A man of leisure, 51 years of age, complained of loss of vitality. His family history was negative; he had been married 25 years and had 3 living and well children. He had had tonsillitis, lues, and gonorrhea in the past and appendicitis 6 months before. Fifteen years before he had been treated for stomach trouble. Aside from his loss of vitality he said he felt well. He stated that he



From the data given above it is evident that this was not a case of diabetes but that the glycosuria was due to a permeable renal filter.*

It is to be noted that the fasting blood sugar was a low normal and that while the blood sugar level rose quickly after the ingestion of glucose, it returned to the normal level in little more than an hour. Sugar was found in the urine throughout the test and it is probable that this man will have glycosuria for the rest of his life. This, however, is of no consequence, and the man should not be put on any restricted diet. It is quite right, however, in such a case, *i. e.*, in the presence of glycosuria, to put the patient on a restricted diet until it is determined whether the glycosuria is due to diabetes or simply to a permeable renal filter.

SUMMARY AND CONCLUSIONS

A series of 12 cases is presented in each of which glycosuria was present. Some of the subjects had a familial history of diabetes, yet not one of them had diabetes. These histories show the importance of making a thorough investigation of any patients who show glycosuria before making the diagnosis of diabetes. They should be treated as diabetics only while the final decision is pending.

A trace of sugar in the urine should always be investigated. In such a case a fasting blood sugar determination should first be made. If this is high, there is a definite basis for diagnosis of diabetes. Only a few hours of treatment will be lost, for the time required is only that elapsing between the time of the examination and the following morning when the blood sugar estimation is made.

If the blood sugar content is normal or only slightly raised the problem is not settled. In such a case a glucose tolerance determination should be made. If the blood sugar returns to the normal level promptly,—within two hours after the injection of 100 gms. of glucose,—the subject is normal; if it returns to the normal level at the end of the third hour, then we are dealing with a prediabetic; if it takes more than 4 hours for the normal level to be reached again, then we are dealing definitely with a case of diabetes, regardless of the fasting blood sugar content.

* John (H. J.), J. Am. M. Ass., 1922, 78, 103-105.

Case No	Fasting												Total Urine Output cc	Total Urine Intake Gms	Total Sugar Intake Gms	Total Sugar Output Gms	Blood Corpuscle Vol at Start, Percent
	1/2 Hour Later		1 Hour Later		2 Hours Later		3 Hours Later		4 Hours Later		5 Hours Later						
	Blood Sugar Mg per 100 cc	Urine Sugar	Blood Sugar Mg per 100 cc	Urine Sugar	Blood Sugar Mg per 100 cc	Urine Sugar	Blood Sugar Mg per 100 cc	Urine Sugar	Blood Sugar Mg per 100 cc	Urine Sugar	Blood Sugar Mg per 100 cc	Urine Sugar					
1	103	2 Plus	184		103	3 Plus	91	Plus	81	Neg			900	100	0 11		51 3/4
2	121	Plus	127		117	Plus	113	Plus	73	Neg			900	100		3 84	41
3	92	Trace	147		70	3 Plus	38	2 Plus	63	Trace			930	100	0 28		
4	103	Trace	123		110	3 Plus	100	Neg	60	Neg			700	100			
5	124	Plus	204		149	2 Plus	50	Neg	83	Neg			900	100	0 06		
6	85	Trace	110		104	Trace	110	Neg	67	Neg			940	100			38 6/10
7	120	2 Plus	174		Trace	Trace	106	Trace	83	Neg			900	100			
8	74	2 Plus	118		98	Trace	70	Neg	67	Neg			795	100	0 1		37
9	75	Trace	117		65	4 Plus	63	Trace	62	Neg			1032	100	0 5		46 3/4
10	80	2 Plus	62		53	Plus	55	Neg	72	Neg			900	100	0 20		40
11	100	Plus	125		108	3 Plus	4 Plus	80	91	Trace			1015	100	0 20		35
12	111	Plus	151		123	2 Plus	2 Plus	77	89	Plus			102	100	1 29		31
					2 Plus	2 Plus	77	Plus	Plus	Plus			178	100	0 77		47

intestinal mucosa with strong soap solutions [Fleig (16)], Witte-peptone [Gley (17)], chloral [Falloise (18)], and other agents. The product extracted is probably in all cases the same [Lalou (19)].

Popielski (20) denied that there is any specific substance present or produced in the small intestine that affects directly the activity of the pancreatic cells. He claimed that the presence of peptones in the blood and a lowering of blood pressure were the effective agents. Many secretin preparations cause a fall in blood pressure. At the same time the volume of blood flow through the pancreas is increased as the result of local vasodilatation which, however, follows rather than precedes the increase in pancreatic secretion and is not necessarily of equal magnitude [May (21), Burton-Opitz (22)]. There is considerable experimental proof that secretin is something separate from the substance that lowers blood pressure. Dale and Laidlaw (23) have succeeded in preparing by a new method a secretin that has powerful action and is relatively free from depressor substance. Launoy and Oechslin (24) have separated two different substances from duodeno-jejunal mucosa. One is an excito-secretory substance, without depressive effect, which stimulates the pancreatic secretion; the other is a powerfully depressing substance, which has little excito-secretory effect. The former is the hormone of Bayliss and Starling and the vasodilatin of Popielski is probably a mixture of both. Matsuo (25) has been unable to obtain a secretin preparation which did not cause some fall in blood pressure, but the degree of the fall and the activity of the various preparations were not at all proportionate. He does not believe that secretin and the depressor principle are identical for the additional reason that acid introduced into the duodenum will produce abundant pancreatic secretion without change in blood pressure.

In 1917 Bickel and his collaborators, Eisenhardt and Bjenab (26), in a series of articles entitled "Ein neues Pflanzensekretin," announced that spinach contains a secretin which acts on both the stomach and pancreas. Similar results were obtained by van Eweyk (27), van Eweyk and Tennenbaum (28), and Bickel and van Eweyk (29). These observations appear to have suggested the possibility of chemical identity or at least similarity of secretin and vitamin. On this point there are a num-

ber of reports of investigations which are in the main negative. Jansen (30) used the anti-beriberi vitamin from rice and found that it does not cause pancreatic secretion and hence is not identical with secretin. Voegtlin and Myers (31, 32) concluded that anti-neuritic vitamin prepared from brewer's yeast and secretin are closely related, if not identical. Cowgill (33) states that extracts of rice polish, wheat embryo, navy bean and yeast gave negative results on pancreatic secretion. Anrep and Drummond (34) and Downs and Eddy (35) have also shown that the idea that water soluble vitamin B and secretin are identical is unsupported by experimental evidence. A recent study of the question by Halliburton and de Souza (36) concludes that secretin extracted from spinach or manufactured by protein hydrolysis does not merit the name, that it has little effect, and can not play any part in digestion.

Accepting as the test for secretin stimulation of the flow of pancreatic juice it was early noted that secretin also increased the flow of bile. This was reported by Bayliss and Starling (6) and confirmed by Falloise (37), Enriquez and Hallion (8), Schäfer (38), who also noted a stimulating effect on the succus entericus, Downs and Eddy (39) and others. This opened the inquiry, which is still going on, as to what other organs or tissues of the body may show an alteration in activity under the influence of secretin.

In 1912 in an article by Alessandro (40) the statement is made that acid macerations of the secretin containing duodenal mucous membrane when introduced into the blood stream cause an increase in the amount of pancreatic juice, lachrymal fluid and aqueous humor secreted, and produce arterial and venous hyperemia of the fundus oculi. Mendel and Treacher (41) and Bainbridge (42, 43) have found secretin to cause an increased flow of lymph from the thoracic duct which is independent of alterations in general blood pressure. Bainbridge thinks this lymph is formed in the pancreas as a result of metabolic changes occurring in that organ during the secretion of pancreatic juice. Pitcarin (44) found that secretin injected into the saphenous vein of an animal of the same species is a diuretic. Abelous and Soula (45) also found that dilute hydrochloric acid introduced into the duodenum or secretin given intravenously increased the secretion of urine. In addition they record increased

secretion. A later report (57) by the same authors was to the effect that in the majority of cases the treatment was without avail. The same conclusion was reached by Bainbridge and Beddard (58), Foster (59) and Dakin and Ransom (60).

Up to the present the only apparent therapeutic uses of secretin are to increase the number of corpuscles in the circulating blood by stimulating the hematopoietic activity of the red bone marrow, and probably to improve digestion by increasing the flow of certain of the digestive juices. If our conception of pernicious anemia as a race between destruction and production of red corpuscles, with the former ultimately outstripping the latter, is correct, then secretin can be of no use. Nevertheless, there are undoubtedly many cases in which the conditions are similar to those existing in the starved rabbits to which reference has been made and in which beneficial results might be expected from the administration of secretin. It is to be hoped that further experimental and clinical studies will be carried out in an effort to define the therapeutic status of secretin.

SUMMARY

The literature on secretin is reviewed.

Personal experiments have shown that secretin has a markedly accelerating effect on erythropoiesis and general nutrition.

It is suggested that these observations may have an important clinical application.

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ON THE OCCURRENCE OF ACCESSORY PARATHY-
ROIDS AND THEIR RELATION TO SURVIVAL
OF ANIMALS AFTER PARATHY-
ROIDECTOMY

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Recently there have appeared in the literature a series of articles (1) (2) (3) (4) (5) (6) (7) (8) (9) in which the authors claim to have controlled and cured tetany in "completely" parathyroidectomized dogs by various procedures. Having worked with parathyroidectomized animals, many of whom failed to show any post-operative symptoms of acute or chronic parathyroid insufficiency, and being aware of the frequent occurrence of accessories, it appeared to us that the statement of these writers, that their dogs were "completely" parathyroidectomized was misleading, inasmuch as it affected the interpretation of their results.

It is the purpose of this paper to present further evidence of the relative frequency of accessory parathyroids in cats, and to point out the possible physiologic rôle played by these masses following the ablation of the main glands.

The parathyroids have four points of origin. They are derived from the third and fourth branchial clefts, in close association with the thymus where development is very complex and the subsequent migration of tissue very marked. These factors greatly increase the possibility of accessories. The relation of migration of organs to the occurrence of accessories is illustrated also by the thyroid and interrenal glands.

Influenced mainly by the development of the thymus, the occurrence of accessory parathyroids may be widespread over neck and upper portion of the thorax. Schaper (10) and Lillie (11) each found masses of parathyroid tissue near

the bifurcation of the common carotid and along the course of this artery in the sheep. Meyer (12) was able to find aberrant glands in all parts of the thoracic thymus of the sheep. Askanazy (13) reports the case of a young man in whom at autopsy an accessory parathyroid was found attached to the phrenic nerve. Thompson and Leighton (14) frequently found parathyroid tissue remote from the thyroid area in dogs. Forsyth (15) identified a parathyroid body hidden behind the sternum.

Supernumerary parathyroids are not uncommon. Klotz (16) found 12 in an adult dog. Thompson and Leighton (14) identified 8 in a dog. In a rat Togofuku (17) found 11 parathyroid masses. Erdheim (18) found 9 in a rabbit, and refers to the case of a man in whom he identified 8 parathyroids. Forsyth (15) was able to demonstrate an equal number in a monkey.

The occurrence of accessory parathyroids is common. In routine examinations of necropsy material, Marine (19) found them in 6 per cent of his dogs. According to Harvier and Morel (20) 50 per cent of cats have accessories, while Farner and Klinger (21) found them in almost all of the cats which they parathyroidectomized. Pépère (22) found accessory parathyroids in most of his rabbits. Erdheim (23) reports finding 4 accessories in a case of infantile myxedema.

By a very crude method we found 12 per cent of a series of cats to have accessory parathyroids within the thoracic thymus area.

PROCEDURE

Forty-two cat thymuses obtained in the routine autopsies in the laboratory, that had been fixed in formalin, for periods varying from a few weeks to about a year, were used. All of the animals were adults. Most of the thymuses had portions of the parietal pericardium and mediastinal lymph nodes attached. Transverse blocks were taken from each thymus and embedded in celloidin. Two sections of about 25 micra were cut from each block, the second section being about $\frac{1}{2}$ of one mm. below the first. The sections were stained with hematoxylin and eosin.

In five (12 per cent) of the animals definite accessory parathyroids were found. In two cats two accessories were found within each thymus.

Undoubtedly if serial sections of the entire thoracic thymus had been examined a much higher percentage of accessory parathyroids would have been found, and if all the structures between the thyroid gland and the arch of the aorta had been sectioned, a still larger number would have been found. The crudity of our procedure emphasizes the frequency of accessory parathyroids.

DISCUSSION

Recent literature challenges the fact that the parathyroids are indispensable to life if the diet is carefully controlled and calcium salts administered. Luckhardt and Rosenbloom claim to have been able to control and cure tetany in "completely" parathyroidectomized dogs by the daily intravenous administration of Ringer's solution for about forty days. Luckhardt and Goldberg report being able to preserve the life of "completely" parathyroidectomized dogs by means of the oral administration of from 0.43 to 2.7 gms. calcium lactate per kilo body weight daily. Dragstedt and Peacock have kept parathyroidectomized dogs alive indefinitely by careful control of the diet, which diet changed the intestinal flora so that aciduric organisms predominated. The latter workers assume a more conservative attitude as to the completeness of their parathyroidectomies. They recognize the possibility that a few parathyroid cells under favorable conditions of diet and environment may function for the whole gland. To determine whether parathyroid removal in a given animal was complete they used the following physiological test: if the animal showed no tetany or depression after about three weeks, it was allowed to eat meat, and "the appearance of severe tetany after 48 hours was taken as an indication of the absence of accessory parathyroid tissue." However, we wish to point out the fallacy of such a test: an animal may have all four parathyroids intact and still show signs of tetany, and further, accessory parathyroid tissue may be frequently demonstrated in the thoracic thymus of cats which died of parathyroid insufficiency, showing tetany or depression or both. As Marine has pointed out "where there is anatomical insufficiency there is also physiological insufficiency, but this is not true conversely."

The work of Luckhardt and Rosenbloom, Luckhardt and Blumenstock, of Luckhardt and Goldberg, and of Dragstedt, and Dragstedt and Peacock emphasizes in an excellent manner the importance of good post-operative care, carefully controlled diet, and the administration of calcium in parathyroidectomized dogs. However, no evidence has been offered to show that the parathyroids are not indispensable to life whether this necessary activity consists of elaborating a secretion or neutralizing a toxin. It appears to us that by their respective procedures they have tided the animals over a critical period for a sufficient length

of time to permit the accessories to hypertrophy. The recurrence of signs of parathyroid insufficiency when an extra load is thrown on the glands or when the general condition of the animal is at all undermined (oestrus cycle, pregnancy, lactation, acid and sulphur administration, constipation) is due to the narrow margin of safety that such animals have when only accessories are functioning. To quote Marine, "in the absence of all parathyroid tissue, calcium salts will not save the animal's life, while in the presence of active parathyroid tissue calcium will save it."

To emphasize further the functional importance of accessories in general, and the extremely small amounts of functionally active tissue necessary for the maintenance of normal behavior under favorable conditions of nutrition and environment, we wish to refer to results following adrenalectomy in rabbits. It has been shown by many observers that in those animals which survive double adrenalectomy for 30 days or longer, accessory interrenal glands can be demonstrated in practically every instance.

We wish to thank Dr David Marine for his assistance and helpful criticism in this work.

CONCLUSIONS

(1) Accessory parathyroids are present in man and animals in a large percentage of cases. By careful examinations of serial sections of the neck and thorax they probably could be demonstrated in almost every case.

(2) No evidence has yet been presented that mammals can survive complete parathyroidectomy.

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III. Über einige menschliche Klemmenderivate.

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Editorial

AN OVARIAN HORMONE

Despite the fact that a tremendous number of articles on the incertory function of the ovary has appeared in medical and scientific journals throughout the world, very little clean cut information is available that can be confidently applied by the medical practitioner in his bedside work. Novak (1), in a critical review recently published in this journal, expressed himself, after years of experience as distinctly uncertain regarding the value of ovarian therapy. Although the feeling is very definite that there is a relation between the ovarian hormone and uterine functions, when one comes to the point of actually prescribing ovarian preparations he is, despite the sweeping claims of some endocrine enthusiasts, shooting in the dark. Occasionally he achieves brilliant success, but often only discouraging failure meets his efforts.

Perhaps the most important item of uncertainty has been the lack of a usable method of assaying ovarian products. While the more reliable manufacturers have done everything in their power to market satisfactory preparations the lack of a suitable standard for testing the efficacy of the preparations has proved a disconcerting obstacle.

For this reason a recent article by Allen and Doisy (2) from the Washington University Medical School at St. Louis on "An Ovarian Hormone," giving a clean cut method of testing its efficacy will be welcomed by endocrinologists throughout the world. The work of Stockard (3), of Long and Evans (4) and of Allen (5) has recently shown that the stage of the estrus cycle of mice, rats and guinea-pigs can be accurately established by microscopic examination of vaginal scrapings. This fact Allen and Doisy utilize in testing the ovarian hormone.

As a source of the hormone Allen and Doisy have used the liquor folliculi from the ovaries of hogs and cattle. It was noted that from 40-48 hours after the injection of this fluid into

mice and rats the animals were in full estrus. This was shown primarily by the condition of the vaginal smears, but the results were checked by an examination of the uterus and the vagina. These were in the typical hyperemic condition characteristic of estrus. When the contained cellular material and fluid proper were separated it was found that the hormone was in the liquid itself. It was found possible to fractionate the follicular liquor so that an apparently protein-free, active substance was obtained.

Not only were the uterine changes of estrus produced, but also growth in the mammary glands. Strikingly, during the induced estrus the animals mated in a normal manner. Some evidence was secured also of hastening of sexual maturity. In case of rats, puberty is marked by the attainment of patency of the vulva. Animals that had been injected with follicular extract attained puberty, as judged by this criterion, 22-40 days before they normally would have done so. At the time of publication the authors had not obtained results from extracts of corpora lutea, of whole ovary, or of the ovarian residue from materials obtained from three of the largest manufacturers of biological products, hence, as uterine or mammary stimulants these were all apparently inert. Further details of this interesting research are promised at an early date.

In view of the ease with which follicular fluid can be obtained and purified this new work suggests fascinating possibilities both from the standpoint of practical therapeutics and of the elucidation of numerous problems in the endocrinology of the female gonads.—R. G. H.

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*Cited from Allen and Doisy (2).

THE BROADER SIGNIFICANCE OF THE DISCOVERY OF INSULIN

The isolation of Banting and co-workers of the specific hormone of the Islands of Langerhans, and its clinical application to the treatment of diabetes mellitus, is universally acknowledged to be one of the most brilliant achievements in medical science and therapeutics. Their steadfast persistence in the face of many obstacles, and despite the discouraging failures of previous workers, merits unstinted praise and congratulation.

So long as efficient use of insulin is restricted to two or more daily injections, and so long as its use orally is futile, there will necessarily remain limitations to its widespread application in treating diabetes. Despite this many thousands of lives will be saved or prolonged that without insulin could not survive; and life will be made more bearable for other thousands, whose carbohydrate tolerance has become so diminished that their meager diet is a severe hardship.

The discovery of insulin includes a wider significance, however, than is noted above. It is to be remembered that the idea of employing pancreatic extracts in the treatment of diabetes mellitus originated many years ago and was a sound concept, based on secure scientific foundations. It had been proven by Minkowski and von Mehring in 1889, that the seat of the disease was in the pancreas. What more natural impulse than to remedy the defective, deficient secretion of the pancreas (more particularly the islet cells) than by administering pancreatic extracts—not only natural, but logical. Murlin, in a recent number of *Endocrinology*, relates the fascinating story of how one after another for over thirty years tried extract after extract, variously compounded and variously administered, only to be disappointed. What was the reaction of the medical profession? Very emphatically and even cynically, that pancreatic organotherapy in diabetes mellitus was both useless and foolish.

When, during these same years, disappointing results followed the use of pituitary preparations, ovarian extracts, testicular substances and adrenal medication in various maladies quite probably due to disease of these glands, where a replacement therapy seemed justified and indicated—then there de-

veloped a very reasonable, but nevertheless profound pessimism for organotherapy in general. Only thyroid extract survived widespread condemnation. Fortunate indeed, for the entire field of endocrinology that one extract remained, whose potency was unquestioned and the administration of which by mouth was so simple and satisfactory.

When, despite these reliable, painstaking reports of failures (with all other gland products except thyroid), a large percentage of the medical profession persisted in indiscriminately and haphazardly prescribing these preparations, even unto pluriglandular ecstasy—the better and wiser portion of the profession became impatient, and the subject of organotherapy sank into deserved disrepute. What a heartening stimulus to the future, what a broad significance therefore attaches to the achievement of insulin! If the true specific hormone of the Islands of Langerhans can be isolated—what is to prevent similar accomplishment for the anterior lobe of the hypophysis, the ovaries, testicles and adrenal cortex? Indeed, there are lights on the horizon already, and a new dawn for endocrinology and humanity seems assured.—H. L.

Book Reviews

HET VITAMINERRAAGSTUK. H. Allacys, Brugge, 1921. Drukkerij Excelsior. 57 p.

A small brochure in Flemish containing an incomplete and confused enumeration of the literature concerning vitamins. Some pages are devoted to the changes observed in the endocrine organs in avitaminosis.—J. K.

SKORBUT. L. Aschoff & W. Koch, Jena, 1919. Verlag G. Fischer, 122 pp.

The magnificent book with its admirable illustrations does not treat specifically of endocrinology, but it reports careful postmortem studies of 23 patients who died from scurvy in which special attention was given to the endocrine organs. The adrenals, pancreas, pineal, thyroid, parathyroids, thymus and testicle were closely examined in all cases. Only the adrenals and the thymus showed changes. In the adrenals the lipid content was high. The thymus generally showed a more marked atrophy than in other persons of the same age under the same conditions.—J. K.

LECONS DE PATHOLOGIE DIGESTIVE. Prof. M. Loeper, Paris, 1919, 4 ed. Masson et Cie. Pp. 298.

These contributions on gastrointestinal pathology are of great value to medical men, especially to specialists who treat diseases of the stomach and the intestines. A fifth volume, of no endocrine interest, was published in 1922; the fourth edition, however, contains two chapters which are of endocrine importance. Dyspepsia of adrenal origin the author describes as a severe form due to adrenal insufficiency. The symptoms consist of slight pains which occur $\frac{1}{2}$ to 2 hours after meals, loss of appetite, constipation, atony of the stomach, loss of flesh, a small amount of hydrochloric acid in the stomach and a small quantity of blood sugar. X-ray examination shows the existence of atony of the stomach and retardation of its emptying power; spasm of the pylorus is rare. In such cases injections of adrenalin are usually very successful. It is impossible to review here the experiments performed on men and animals showing the influence of the

adrenals and of adrenalin on the alimentary canal. I shall mention only that the author speaks of "insuffisance surrénale" as if its existence were certain; however, according to other investigators there seems to be more evidence against than in favor of the existence of such a disease. In his chapter on gaseous dyspepsia in patients with goiter the author points out that gastrointestinal disturbances are not rare in Graves' disease. The influence of the thyroid on the functions of the stomach has had little investigation; however, cases have been reported of *aërophagia* and of spasms of the oesophagus which seemed to be of thyroid origin and which rapidly improved when the thyroid was treated. Simple goiter with dyspepsia is also observed frequently. In explanation of these facts the author suggests a relation between the thyroid and its hormone on one hand and the involuntary nervous system on the other. Most stomach trouble found in diseases of the thyroid, however, originate in meteorism, due to *aërophagia*. The *aërophagia* is attributed to spasm of the muscular wall of the stomach, caused by irritation of the vagus. This is often combined with an increased irritability of the muscles in hyperthyroidism. In this way mechanical as well as toxic forms of stomach trouble in diseases of the thyroid may be explained.—J. K.

LA QUESTION DES VITAMINES. Dr. G. Houllbert, Paris, 1921.
Librairie Arnette. 91 p.

Although this book is primarily concerned with vitamins, a considerable amount of material of endocrine interest is included, despite the fact that the text shows that the author is entirely unfitted to deal with such topics. For example, he lays much stress on a theory that function of the endocrine organs depends on the presence of vitamins. This is a type of facile generalization that has brought so much ridicule upon the literature of endocrinology. Even on the subject of the vitamins, themselves, the author is superficial and inaccurate. Although the book has received considerable favorable notice, in the opinion of the reviewer it is most noteworthy as an example of biological dilettantism.—J. K.

THE ANATOMY AND PHYSIOLOGY OF THE CAPILLARIES. Prof. August Krogh, Yale University Press, New Haven, 1922, pp. 276.
Illus.

This book contains the lectures given by Professor Krogh at Yale under the Silliman Foundation. Their clear conciseness makes them admirable reading. The absence of technical terminology comes as a pleasure to the specialist in other fields.

In addition to consideration of the distribution, contractility, structure, innervation, reaction to stimuli and permeability of the capillaries a chapter is devoted to the hormone control of this portion of the vascular system. The presence of an unknown substance in the blood, a function of which is concerned in the regulation of capillary contractility, is demonstrated. This substance has been termed the x-hormone. The effects of *pituitary* extracts upon capillary activity are described in some detail and the preliminary hypothesis is advanced that the x-hormone is produced by the pars nervosa or pars intermedia of the *hypophysis*. Reference to the effects of other endocrine products are to be found scattered throughout the lectures. The volume is to be commended both to the practitioner of medicine and to the scientist.—F. S. H.

CLINICAL TREATISE ON DIABETES MELLITUS. Marcel Labbé. Translated, revised and edited by C. G. Custom. William Wood & Co., N. Y., 1922. 382 pp. \$5.

Cited, Chem. Abst., 17, 1073.

DIE KRETINISCHE ENTARTUNG. Dr. Ernst Finkbeiner, Berlin. 1923. Springer. Pp. 432. Illus.

This monograph attacks the problem of the cretin from the point of view of anthropological measurements. Intensive studies were made of the long bones and skulls of cretins and their deviations from the normal are well described. As a compilation of the existing data on cretinism the monograph is a valuable contribution. Cretinism is defined as a form of endemic degeneration of European peoples. Its causal agent is mainly heredity. Hypothyreosis is considered as an accompaniment, not a cause of the condition. The arguments supporting this point of view are extremely weak and even the observational data would not bear critical analysis since the comparative measurements are too few to allow such a definite and far-reaching conclusion. Space is lacking for a consecutive analysis of the fallacious opinions expressed. When an author starts out with the idea that animal experimentation can never throw light on the problem of cretinism he naturally omits reference and study of the observations obtained from such investigation. Notwithstanding these defects, which after all have their use in that they are stimulative of thought, the monograph serves a good end in bringing together many scattered data on a subject of importance.—F. S. H.

SEX AND DEVELOPMENT OF SEX CHARACTERS. M. Zawadowsky, Moscow, State edition, 1922. 255 pp., with 20 colored plates and 94 figures in the text. Russian with 20 pages of German summary.

The author has performed during 1919 and 1920, under the incentive of Steinach's feminization and masculinization experiments, an extensive series of experiments with castration, feminization, masculinization and hermaphrodization in the fowl. There were 109 experiments on fowl, 14 experiments on pheasants and 3 on ducks. He fully confirmed the results of Goodale and of Pézard. The castrated cock and the castrated hen were exactly alike. Like Tandler, Pézard and Lipschütz, the author concludes that there is an asexual type and that those characters which, like the plumage and the spurs of the cock, are independent of the sex gland, represent characters of this asexual type. Castration experiments on pheasants gave similar results. The statements of Goodale were confirmed in feminization and masculinization experiments. The conclusion is drawn that the tissues of the male and female are at the beginning identical and that they undergo male and female differentiation only under the influence of sex hormones. The statements of Zawadowsky made on the appearance in castrated hens of male characters which depend on sex hormones, as the male comb and sexual instincts, are of great interest. In these experiments a development of the right-sided ovarian rudiment was seen. Also these experiments fully corroborate those of Goodale and of Pézard. Zawadowsky suggests that the ovary has also a "hetero-sexual potency." In agreement with what was observed by Goodale, the author stated that testicular grafts into *normal* hens were mostly unsuccessful. The graft took in only one out of 6 cases. In two cases the testicular graft took, though the ovary was regenerated. There was in these cases hypertrophy of the comb, but the latter was not so erectile as in the normal cock. The testicular graft had no influence on other sex characters, as sexual instincts and plumage, even when the generative part of the testicle was developed. On the contrary, transplantation of ovary into normal cocks caused feminization as to the plumage. In order to study whether the sexual hormones of different species are identical the author transplanted into castrated cocks of different species sex glands of pheasants. These experiments could not be finished on account of political events in Russia; but they indicate, nevertheless, that there is no "species specificity" of sexual hormones.

The observations of Zawadowsky on castrated mammals are also of great interest. He observed different castrated specimens of antelopes in the great zoological park of Nova-Ascania in

Southern Russia (*Portax-Pictus*, *Cervicapra*, *Conochetes Gnu*, *Cervus Lama*, *Capreolus Caprea*). There is in the male *Portax-Pictus* after castration a transformation of the grey male coat into the brown female one; the transformation takes place at the first moult after castration. If horns have already grown when castration is performed, they are preserved. Zawadowsky concludes that also in manumals there is a soma identical for both sexes. In many places he speaks of an identical soma, at other places of an equipotential soma. He fully agrees here with the suggestion Lipschütz made on this question in different papers in 1918 and 1919. The term "equipotential soma" might be more convenient than the term "asexual soma" that Lipschütz used as being less extreme and leaving the door open for changes which might become necessary on account of new facts.

Zawadowsky reports also on experiments on sex limited inheritance from a hormonal aspect. In 1919 Lipschütz attempted to explain from a hormonal aspect the fact that female sex characters are transmitted by the father and male characters by the mother. It was assumed that the parent transmits to its offspring the characters of the asexual type, i. e., the capacity to react to sexual hormones in a manner characteristic for a given species; so the parent always transmits the capacity to react both in a male and a female manner; it depends upon the sex specific hormones of the offspring whether the reaction of the soma will be male or female. In crossing experiments the male generative cells will transmit characters of the asexual soma of the strain of the father and by this the capacity is transmitted to react to female hormones in a manner characteristic for the *female* of the *father's* strain and *vice versa*. A full confirmation of Lipschütz' point of view is given by some experiments of Zawadowsky. He crossed a black male Langshan with a female barred Plymouth Rock; there were in the first generation barred cocks and plain black hens. Castration of the black hen of the F_1 then caused the appearance of the male plumage of a Langshan cock and not of that of a Plymouth Rock cock. Evidently the females of the F_1 inherit the characters of the neutral form of the strain to which the male parent belongs.

The author's classification of sex characters is very similar to that of Pézard and of Lipschütz, though he has not taken into consideration the literature from 1913 and 1922. Zawadowsky gives important, independent experimental evidence for many of the theses of Steinach, Sand, Goodale and Pézard, and in addition, some new experimental facts. The experiments related in the book are extremely numerous; full protocols with photographs and complete numerical data are given. (A statement in the German summary appears to have been misleading on this point.)

The experiments have been carried out under most difficult circumstances and the author deserves great admiration for having continued scientific work. His experiments were performed in the zoological park of Nova-Ascania in Southern Russia between the Red and the White fronts under the constant oppression of corrupt military forces.—A. Lipschütz.

Abstract Department

(ADRENALIN, HYPOPHYSIS.) The effect of various other factors than blood urea concentration on the rate of urea excretion. Addis (T.) & Drury (D. R.), *J. Biol. Chem. (Balt.)*, 1923, 55, 629-638.

In rabbits all the changes in the rate of urea excretion which cannot be explained by variation in blood urea concentration may be experimentally duplicated by the subcutaneous injection of adrenalin and of pituitrin. Those rates which are greater than the blood urea concentration would warrant can be produced by adrenalin, and those which are lower by pituitrin. Further, these substances, as far as their renal action is concerned, are directly antagonistic, for if the appropriate doses of adrenalin and pituitrin are mixed together before they are injected the rate of urea excretion is unchanged. The results induced by pituitrin in rabbit can be reproduced in man. In man it is not feasible to reproduce all of the adrenalin effects. It differs from pituitrin in that with increasing doses there comes a point where the augmenting influence on the rate of urea excretion becomes less marked, and as the dose is increased the effect is reversed and the rate is decreased.

—F. S. H.

Spasm and ADRENALIN. Aiya (T.), *Jikwa Zasshi*, 1922, No. 268 (Sept.), abst., *Jap. Med. World (Tokyo)*, 1923, 3, 37, 53.

After injecting adrenalin into more than 60 subjects with ekiri and dysentery, the author decides that the change in the suprarenal capsule is not an important factor in the development of spasm.

—R. G. B.

Cholesteremia and the ADRENAL glands in the rabbit (*Sui rapporti fra colesterina e capsule surrenali nel coniglio*). Alessandri (C.), *Riv. crit. di clin. med. (Firenze)*, 1921, 22, 397, 409.

(ADRENALS) Three cases of cutaneous discoloration—two of Addison's disease and one of hemolytic jaundice. Anders (J. M.), *Med. Clin N. Am. (Phila.)*, 1923, 6, 849-859.

A report of 2 cases of Addison's disease with remarks on differential diagnosis.—I. B.

Three cases of acute and subacute ADRENAL insufficiency following malaria (*Trois cas de insuffisance surrénale aiguë et subaiguë consécutifs au paludisme*). Antonin (P.), *Marseille Méd.*, 1922, 59, 68-73.

Digitalin and ADRENALIN-CHLOROFORM syncope (Digitaline et syncope adrénalino-chloroformique). Bardier (E.) & Stillmunkes (A.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 593-594.

Excitation of the splanchnic nerve in the dog. Attempt to dissociate the effects of the vaso-motor fibers from those of the ADRENALIN secreting fibers (Excitation du nerf splanchnique chez le chien. Essai de dissociation des effets de cette excitation sur les fibres vasomotrices et adrénalino-sécrétrices). Barillet (H.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 509-510.

Effects of optical isomers of ADRENALIN bases on glycemia (Effets de bases adrénaliques isomères optiques sur la glycémie). Bierry (H.), Rathery (F.) & Levina (Mlle. L.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 3-5.—T. C. B.

Influence of the ADRENAL glands on DIABETIC hyperglycemia (Influences des glandes surrénales sur l'hyperglycémie diabétique). Boeggild (D.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 816-818.

(ADRENALS) Scleroderma. Bolten, *Nederl. Tijdschr. v. Geneesk. (Haarlem)*, 1922, 66 (II), 2981-2984.

Bolten considers scleroderma as due to insufficiency of the adrenals, and the low blood pressure, the cardiovascular asthenia, the pigmentation and other symptoms seem to uphold this theory. Cases are reported in the literature of a combination of scleroderma and Addison's disease. In some cases differential diagnosis between these two diseases may be impossible. However, as cases of scleroderma with Graves' disease have also been described, it is possible that scleroderma does not always have the same cause.—J. K.

Analgesic power of ADRENALIN (Le pouvoir analgésique de l'adrénaline). Bonnefon, *Gaz. hebdomadaire de médecine de Bordeaux*, 1922, 43, 94.

The use of adrenalin 1:1000, in ophthalmic toxic neuralgia just before the crisis is beneficial. With injection at the beginning the crisis is shortened without becoming less acute; injection during the crisis has no effect.—F. S. H.

ADRENALIN and chronic glaucoma. Ocular hypertension by vaso-constriction (Adrénaline et glaucome chronique. L'hypertension oculaire par vaso-constriction). Bonnefon, *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 433-434.

Sudden death due to ADRENAL insufficiency. Probable adrenal encephalopathy (Mort subite par insuffisance surrénale. Encephalopathie surrénale probable). Bonnin, Secousse & Ichon, *Gaz. hebdomadaire de médecine de Bordeaux*, 1922, 43, 82-83; see also, *J. Méd. de Bordeaux*, 1922, 52, 191.

Tuberculosis of adrenals was observed. Two days before death the patient had hemiplegia and difficulties with speech, followed by hemiparesis.—F. S. H.

Total caseous tuberculosis of the ADRENALS with adrenal insufficiency of rapid development; no pigmentation (*Tuberculose caséuse totale des surrénales avec syndrome d'insuffisance surrénale à marche rapide sans pigmentation*). Bouchut, Gensollen & Morénas, Soc. méd. d. hôp. de Lyon, 1922, Dec. 5; abst., Presse méd. (Par.), 1922, 30, 1078.

The authors report the case of a man of 25 years, with a previous history of tuberculosis, who was taken suddenly, in the midst of a period of asthenia and weakness, with an acute attack, similar to intoxication or peritonitis. The suffering was intense; the arterial tension was low, 55/25. No pigmentation of the skin or of the mucous membrane was seen. Death occurred in a very short time. At autopsy tuberculous granulations were observed on the lungs; the 2 adrenals were entirely transformed into shells comprised of caseous pus, no normal structure being present. This acute form of adrenal insufficiency is similar to cases reported by Sergeant and Léon Bernard. Such pseudo-peritoneal manifestations are well known, although rare, and are not usually accompanied by visible pigmentation.—R. G. H.

ADRENAL insufficiency of rapid termination (*Insuffisance capsulaire à terminaison rapide; absence de mélanodermie; lésions caséuses massives des surrénales*). Cade & Barbier, Soc. méd. d. hôp. de Lyon, 1922, Dec. 5; abst., Presse méd. (Par.), 1922, 30, 1078.

A case is reported of adrenal insufficiency which developed rapidly in 3 or 4 months. No pigmentation, cutaneous or mucous, was seen. There were purulent lesions of the two adrenals which were so extensive that no part of the gland could be recognized, even at histologic examination. There were also extensive pericapsular lesions, and, as usual, it was impossible to know to what cause to attribute the asthenia and hypertension; neither could it be explained why melanoderma did not exist in this case.—R. G. H.

Absorption and action of ADRENALIN (*Über Adrenalin-Resorption und Adrenalin-Wirkung*). Cahn (R.), & Steiner (B.), *Jahrb. f. Kinderh.* (Berl.), 1922, 99, 44-48.

In children in whom subcutaneous adrenalin injections produce a rise in the blood pressure, a rise in the blood sugar invariably occurs. A marked rise in blood sugar is also produced in children in whom no rise in the blood pressure follows the injection. In such children intravenous injection of adrenalin does not produce a pressure rise. Variations in absorption of the adrenalin are not, therefore, the cause of the variation in the response, as Csepai has

suggested from a study of the blood pressure reaction. Apparently a dissociation of the actions of adrenalin on blood pressure and blood sugar exists.—Med. Sc., 7, 528.

The brain and ADRENAL function (*Das Gehirn und die Nebennierenfunktion*). Ceni (Carl), Arch. f. Entwcklungsmechn. d. Organ. (Berl.), 1921, 49, 491-509.

Extirpation of one or both cerebral hemispheres in the pigeon causes hypertrophy of the adrenals in direct proportion to the trauma. This is noticeable on the fifth or sixth day after the operation and is maximal about the thirtieth to fortieth day, amounting to as much as three or four times the usual volume of the gland. There is a simultaneous atrophy of the gonads as a whole, but hypertrophy of the interstitial cells. Histologically both the cortex and medulla of the adrenals show hypertrophy and hyperplasia of both glandular parenchyma and stroma. These changes are accompanied by dysfunction of the adrenals. The staining reaction with hematoxylin and the chromaffine reaction of the medulla are partly lost. All these changes are considered to be due to the destruction of special centers in the brain. Reintegration of the adrenals may gradually occur parallel with the restitution of the sexual glands.—A. T. R.

(ADRENALIN) The influence of some pharmacodynamic agents on the oculo-cardiac reflex and on the solar reflex (*Influence de quelques agents sur le réflex oculo-cardiaque et le réflex solaire*). Claude (H.), Tinel (J.) & Santenoise (D.), Compt. rend. Soc. de biol. (Par.), 1922, 87, 1347-1349.

The subcutaneous injection of 1 mg. of adrenalin causes the solar reflex to appear in a subject in whom compression of the abdomen had no effect. The accentuation of the solar reflex is clearer than with atropin, whereas the frequently observed diminution of the oculo-cardiac reflex is very feeble. The preponderating action is excitation of the sympathetic system.—T. C. B.

Antagonism between ADRENALIN and cinchona. Clerc (A.) & Pezzi (C.), Arch. d. mal. du cœur [etc.] (Par.), 1923, 16, 1-16.

Clerc and Pezzi extended their former studies on the antagonism between epinephrin and quinin on quinidin, cinchonin and cinchonidin in which they found a similar action to quinin. They all paralyze the bulbar center of the pneumogastric nerve, while epinephrin excites it. The acceleration of the heart action caused by small amounts of these drugs is due to excitation of the accelerators, not to paralysis of the pneumogastric, which requires larger doses.

—J. Am. M. Ass., 80, 1180.

ADRENALIN and tuberculosis (*Adrénaline et tuberculose*). Colbert & Durand, Gaz. hebdomadaire de médecine de Bordeaux, 1922, April 23; abst., Arch. méd. belges (Brux.), 1922, 75, 631.

The rôle of adrenalin in the treatment of tuberculosis was studied. Adrenalin differs in action from the pharmaco-dynamic and from the quantitative points of view; of natural adrenalin (levogyrous) and synthetic adrenalin (levogyrous and dextrogyrous) the levogyrous variety alone is active. The authors do not particularly recommend either kind, but advise the continuous administration of the same product in any given subject. The intravenous method of administration should not be used except in extreme cases. Although theoretically the digestive juices modify the composition of the adrenalin, administration by mouth is advised. In this case, however, it should be given in large doses at intervals of 2 hours daily at the utmost.—R. G. H.

(ADRENIN) The free sugar in the liver and its significance for carbohydrate metabolism. Cori (K. F.), Poucher (G. W.) & Cori (G. T.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1923, 20, 522.

The influence of adrenin and Iletin on the free sugar content of the liver and the blood sugar is described.—J. C. D.

ADRENAL insufficiency and the incoercible vomiting of pregnancy (*Insuffisance surrénale et vomissements incoercibles de la grossesse*). Crousse (R.) & Leyman (F.), *Ann. de l'Inst. chir. de Brux.*, 1921, 22, 10-16.

Solution of ADRENALIN for injections (*Solution d'adrénaline pour injections*). Debucquet (L.), *J. de pharm. et chim. (Par.)*, 1922, 25, 136-319; abst., *Ber. ü d. ges. Physiol. (Berl.)*, 1922, 14, 192.

The author introduces for the preparation of adrenalin solution a saturated aqueous benzoic acid solution. A method of preparation is described.—R. G. H.

The importance of the ADRENAL glands in the action of pilocarpine, physostigmine and strychnine. Edmunds (C. W.), *J. Pharmacol. & Exper. Therap. (Balt.)*, 1923, 20, 405-418.

The effects of pilocarpine, physostigmine and strychnine upon cat's uterus and intestine were studied in the presence of the adrenal glands and after their removal. The author concludes that the increased epinephrin output following the administration of these drugs may very considerably alter their action.—G. E. B.

The effect of EPINEPHRIN upon the blood picture. Edmunds (C. W.) & Stone (Ruth P.), *J. Pharmacol. & Exper. Therap. (Balt.)*, 1923, 21, 210-211.

The response of the rabbit to epinephrin was found to be similar to that of the dog as regards effect upon the hepatic vein, portal pressure and liver volume. In dogs elimination of the liver from the circulation did not alter the polycythemia produced by epinephrin. Ergotoxin prevented the increase in red blood cells. The

authors suggest as a probable explanation of the polycythemia the action of epinephrin upon the bone marrow.—G. E. B.

Changes in the ADRENALS after ablation of the liver (Nebennierenbefunde nach Leberexstirpation). Elias (H.), *Klin. Wchnschr.* (Berl.), 1922, **1**, 1948.

After liver extirpation in animals the principal symptoms are adynamia, hypoglycemia and diarrhea, symptoms which are also found in Addison's disease. To explain these symptoms we must think of hypoglycemia as being caused by destruction of the most important quantity of glycogen in the body. Administration of sugar, therefore, should improve temporarily the condition of the animal. In Elias' experiments, however, no improvement was noted when sugar was injected intravenously in animals without a liver. The author tried to determine whether, as in Addison's disease, changes in the adrenals after ablation of the liver were responsible for the adynamia. He found that the adrenals contained only about one-third of the adrenalin found in normal animals; in most cases the adrenals showed a very slight staining with chromates after the operation. Section of the splanchnic prevented these changes. The author states that it is probable that the changes in the adrenals after ablation of the liver are caused by nerve impulses.—J. K.

ADRENALS and antigens (Nebennieren und Antigene). Emmerich (E.), *Verhandl. d. deutsch. path. Gesellsch.* (Jena), 1921, **18**, 213-215.

See *Endocrin.*, **6**, 122.

Malignant disease of the ADRENALS with report of a case. Fuller (H. G.), *J. Urol.* (Balt.), 1922, **7**, 77-85; see also, *Tr. Am. Ass. Genito-Urin. Surg.* (Balt.), 1921, **14**, 227-235.

A brief case report.—J. C. D.

Action of repeated subcutaneous injections of ADRENALIN on the rabbit (Etude de la glycosurie adrénalinique—action de la répétition des injections sous-cutanées d'adrénaline chez le lapin). Garnier (M.) & Schulmann (E.), *J. de Physiol. et de path. gén.* (Par.), 1923, **21**, 92-103.

Repeated small injections of adrenalin are well borne by rabbits. They become accommodated to toxic doses if the doses are progressively increased; thus amounts which would produce death in a few hours will be perfectly well tolerated. The tolerance persists for some time after stopping the injections. Repeated injections after interruption cause a marked wasting. Under the influence of small doses repeated for a long period, glycosuria diminishes and disappears, but each injection is followed by hyperglycemia, as marked for the last as it was for the first doses. This is true for some animals. For others glycemia permanently increases so that

there is increased glycosuria. Death may occur under these conditions. If one injects increasing quantities of adrenalin the strong doses do not cause more marked hyperglycemia than the weak.

—W. B. C.

Section of the splanchnic and ADRENALIN glycosuria in the frog (Section du splanchnique et glycosurie adrénalique chez la grenouille). Gautier (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1400-1401.

Destruction of the splanchnic and its ganglia does not prevent the glycosuria caused by injection of adrenalin in the frog.—T. C. B.

Successive action of eserine and ADRENALIN on the pupil of the frog's eye in vivo (Actions successives de l'ésérine et de l'adrénaline sur la pupille de l'oeil de grenouille, in vivo). Gautier (C.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1402-1403.

In the frog adrenalin dilates the pupil to its maximum after myosis has been induced by eserine, but eserine is without effect when the pupil has been dilated by adrenalin.—T. C. B.

ADRENALECTOMY in the frog (La produzione di calore nella rana in diverse condizioni sperimentali. Nota V. Researches alla rana privata delle capsule surrenali). Gayda (D. T.), *Arch. di sc. biol. (Napoli)*, 1923, **4**, 93-105.

The author experimented on both partially and completely adrenalectomized frogs. In both cases the production of heat decreased immediately from 30 to 40%. After this diminution, in the animals in which the adrenal glands were completely destroyed the diminution of heat continued until death resulted. In the case of partial destruction of the adrenal glands, the diminution stopped for a time and then went on until death resulted. In both cases the author attributes the first diminution of heat to the result of the operation. In cases of complete destruction the second diminution of heat was due, according to the author, to the disappearance of the tonic excitement of the sympathetic system, to the alteration of the material change of the hydrocarbons, and finally to the phenomenon of asthenia and muscular weakness. The behavior in the production of heat in the case of the partial removal of the adrenal glands shows that the parts of the adrenal glands which remained intact were able for a time to compensate for the destruction of the other parts. After a while the remaining parts also probably suffered necrosis.—A. C. M.

Fats and lipoids of the cortex of the ADRENAL in fasting animals (Grassi e lipoidi della corteccia surrenale nel digiuno). Giglioli (B.), *Arch. per le sc. med. (Torino)*, 1922, **45**, 24.

In fasting animals the lipoids of the cortex of the adrenal are diminished. The great quantities of sudanophil material which

under such conditions are seen in the same situation are not lipoids, but either neutral fats or cholesterol derivatives. Their almost violet color in specimens stained by Nile-blue sulphate is very much in favor of the second supposition.—Med. Sc., 8, 59.

Technic of ADRENALECTOMY (Zur Technik der Nebennierenexstirpation). Girgolaß (S. S.), Zentralbl. f. Chir. (Leipz.), 1922, 49, 1361-1363.

Consequences of the destruction of the ADRENALS in the toad and in the frog [Consecuencias de la destrucción de las capsulas suprarenales en el Bufo marinus (L) Schneid y el Leptodactylus ocellatus (L)]. Giusi (L.), Rev. Assoc. méd. argent. (Buenos Aires), 1921, 34, 15-19 (Sec. Soc. de Biol.).

See Endocrin. 5, 782.

Fatal doses of various poisons in ADRENALECTOMIZED and HYPOPHYSECTOMIZED toads (Dosis mortales de varios venenos en sapos suprarrenoprivos e hipofisioprivos). Giusti (L.), Rev. Assoc. méd. argent. (Buenos Aires), 1921, 34, 36-43 (Sec. Soc. de Biol.).

The sensibility to toxins is normal in toads without the hypophysis. In adrenalectomized toads, however, there is greater sensibility to morphin and veratrin but less to atropin and curare.

—B. A. H.

The vascular relations of the ADRENALS and their physiological value from the point of view of the suprarenal secretion of adrenalin (La fonction des surrénales—V. Les relations vasculaires surrénéo-rénales et leur valeur physiologique au point de vue de la sécrétion surrénale d'adrénaline). Gley (E.) & Quinquaud (A.), J. de Physiol. et de path. gén. (Par.), 1921, 19, 504-514.

The authors discuss the evidence of anastomoses between the adrenal venous trunk and the perirenal plexus. They confirm earlier observers in finding that anastomoses are present, but declare that they are rare and of relatively little importance. Nevertheless, they admit that double adrenalectomy is preferable to ligation of the lumbo-adrenal veins if one desires to suppress adrenal function.—W. B. C.

Action of ADRENALIN on the THYMUS (Action d'adrénaline sur le thymus). Goldner (J.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 545-548.

A histological description of the thymus after daily injections of adrenalin for 30 days, with the conclusion that there is here an interglandular relation.—T. C. B.

(ADRENALIN) Alterations of the H-ion concentration in the blood of the portal vein and the vena hepatica (Untersuchungen über den Mechanismus der Adrenalinhyperglykämie. I. Mitteilung:

Ueber Aenderungen der Wasserstoffionenkonzentration im Blute der Pfort-ader und vena hepatica). Gottschalk (A.) & Pohle (E.), Arch. f. exper. Path. u. Pharmakol. (Leipz.), 1922, 95, 65-74.

Adrenalin hyperglycemia is the consequence of passive hyperemia in the liver (Neubauer), caused by the adrenalin and at the same time by a formation of acid, especially lactic acid, in the blood (Elias), and of the effect of these 2 factors upon the liver. Experiments were performed on rabbits. Blood was taken by heart puncture and out of the liver vessels. Adrenalin was administered subcutaneously and as a continuous intravenous infusion. Determination of the H-ion concentration was made by a gas chain. Perfusion of isolated livers with blood containing adrenalin changed the H-ion concentration only if adrenalin were added in amounts larger than are usually found in living animals. Acidification is due, therefore, to no direct alteration of the serum by adrenalin, but a complex occurrence in the entire organism. Application of adrenaline in doses which cause hyperglycemia caused considerable increase of the H-ion in the portal blood and still more in the blood of the vena hepatica. After adrenalin injection the increase of blood sugar began 10-20 minutes sooner than the H-ion increase in the portal blood. Hyperglycemia endured more than 4 hours longer than the H-ion augmentation in the portal blood. It is possible that the H-ion increases relatively late in the portal blood because the carbonates are formerly saturated with CO_2 .—A. B.

(ADRENALIN) Is there a genetic connection between the change of H-ion concentration in the liver stream and hyperglycemia? (Untersuchungen über den Mechanismus der Adrenalinhyperglykämie. II. Mitteilung: Besteht ein genetischer Zusammenhang zwischen der Aenderung der Wasserstoffionenkonzentration im Leberstromgebiet und der Hyperglykämie?). Gottschalk (A.), & Pohle (E.), Arch. f. exper. Path. u. Pharmakol. (Leipz.), 1922, 95, 75-92.

Temporary compression of the portal vein in rabbits causes increase of the H-ion concentration within this vessel and distinct hyperglycemia. This is probably a consequence of local acidosis, for alkali taken by mouth (Ca. 100 cc. of a 5% solution of NaHCO_3) diminishes the hyperglycemia considerably without surmounting the physiological degree of alkalescence in the portal vein blood. Temporary ligation of the vena porta 15 minutes after subcutaneous adrenalin injection causes a decided check of the blood sugar increase during the closure. Injection of adrenaline during ligation of the portal vein does not influence the blood sugar. Peroral administration of a bicarbonate solution in a concentration which does not destroy the adrenalin markedly hinders the adrenalin hyperglycemia without altering the H-ion in the portal blood. Even the H-ion concentration of the liquids in the liver tissue seems to be augmented by adrenalin, for the H-ion increases within the vena

hepatica much more than in the vena porta, although arterial blood is continually flowing into the liver. The authors conclude that the increase of the H-ion concentration in the portal blood and in the liver caused by adrenalin is one of the conditions which effects adrenalin hyperglycemia, probably in such a way that the acidity causes a swelling of the liver cells in which the adrenalin tends to cause a reaction between glycogen and diastatic ferment.—A. B.

The effect of EPINEPHRIN on excised strips of frogs' digestive tracts. Gruber (C. M.), *J. Pharmacol. & Exper. Therap.* (Balt.), 1923, **20**, 321-357.

The activity of the digestive tracts of recently caught and starved frogs is entirely similar. The longitudinal muscle of the esophagus is more sensitive to adrenalin than the circular muscle. Weak solutions produce tonic contraction of both coats of the esophagus, increase the tonus and in some cases the rate and force of contractions of both coats of the stomach, small intestine, rectum and cloaca. Stronger solutions produce relaxation in all these organs. What appeared to be the cardiac and pyloric sphincters responded in like manner; the ileocolic sphincter sometimes responded similarly, but in most cases it was thrown into tonic contractions by strong as well as weak concentrations. Strips taken from different parts of the small intestine responded similarly to equal concentrations of adrenalin. The lower part of the alimentary canal appears to be more sensitive to adrenalin than the circular muscle of the esophagus. The author concludes that the thoracic-lumbar autonomic nervous system must supply all the organs and sphincters except possibly the ileocolic with both tonic augmentative and inhibitory nerve fibers.—G. E. B.

Action of ADRENALIN on the striated muscular system (Acción de la adrenalina sobre el sistema muscular estriado). Guglielmetti (J.), *Rev. Asoc. méd. argent.* (Buenos Aires), 1922, **35**, 324-328.

See *Endocrin.*, **7**, 103.

(ADRENALIN) Severe vomiting of pregnancy (Un cas de vomissements graves au cours de la gestation). Guillemet (P.), *Gynéc.* (Par.), 1923, **22**, 111-112.

Report of the beneficial results of treatment by adrenal extract. Six capsules containing 0.1 gm. of Choay's preparation were given.

—F. S. H.

(ADRENIN) A study of the pulmonary circulation by the transillumination method. Hall (H. L.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, **20**, 483-485.

Pithed cats were used. Among other observations the author noted a decrease in the size of the pre-arterioles and arterioles after injections of adrenin.—J. C. D.

The internal secretion of ADRENALIN and its significance in pathology (Sur la sécrétion interne d'adrénaline et son intérêt pour la pathologie). Hallion (L.), Rev. prat. de biol. [etc.] (Par.), 1922, 15, 1-8.

The action of ADRENALIN in the DEPANCREATIZED dog (Action de l'adrénaline chez le chien dépancréaté). Hédon (L.), Soc. d. sc. méd. et biol. de Montpellier [etc.], 1923, March 23; abst., Presse méd. (Par.), 1923, 31, 340.

From the results of 2 experiments performed on totally depa-creatized dogs (later verified at autopsy) which presented normal diabetes, it was concluded that the subcutaneous injection of adrenalin causes increased hyperglycemia and glycosuria. The D/N ratio was much higher than in ordinary experimental pancreatic diabetes.—R. G. H.

ADRENALIN and the blood picture (Suprarenin und weisses Blutbild). Hess (F. O.), Deutsches Arch. f. klin. Med. (Leipz.), 1922, 141, 151-164; see also, Klin. Wchnschr. (Berl.), 1922, 1, 147; abst., Ber. ü. d. ges. Physiol. (Berl.), 1923, 18, 359.

ADRENALINEMIA (Zur Adrenalinaemie Frage). Hess. (O.), München. med. Wchnschr., 1922, 69, 1297-1300.

The author examined the blood of healthy persons and of several patients. In the peripheral arterial or venous blood he found neither adrenalin nor any substance with vasoconstrictor properties.—J. K.

ADRENALS) Malignant hypernephroma in childhood. Hoag (L. A.), Am. J. Dis. Child. (Chicago), 1923, 25, 441-454.

A girl of 4 1/4 years gave a history of 3 convulsive attacks followed by periods of lethargy within the month prior to admission. She was apathetic; the facial expression was stolid; the eyes staring; the voice deep; and she had a prominent mons veneris, large labia minora and majora and a clitoris of adult size with a redundant prepuce. Hypertrichosis was of the male type of distribution. The breasts were normal. Examination showed a tumor of the right flank. Postmortem findings showed a malignant hypernephroma of the right adrenal cortex; arterio-sclerosis of the pial vessels, multiple superficial cortical softening of the brain, and pathological cellular accumulation in the region of the stalk of the pituitary; the thyroid, which was normal, was small with abundant colloid; the ovaries showed an unusual number of large cystic follicles but no evidence of menstruation. A review of the literature is appended.—M. B. G.

(ADRENALIN) Pharmacology of the involuntary nervous system (Zur Pharmakologie des vegetativen Nervensystems). Hoffmann (R.), Wien. Arch. f. inn. Med., 1923, 3, 543-552.

The author studied the influence of different combinations of pilocarpin and adrenalin on perspiration, salivation, and sugar metabolism. He concluded that the effect depends on the state of irritability of the involuntary nervous system caused by the injection of the first drug, and that the quantity and the method of administration of the second drug is of no real importance.—J. K.

(ADRENALIN-PITUITRIN) The pigmentary effector system. II. Hogben (L. T.) & Winton (F. R.), *Proc. Roy. Soc. (Lond.)*, 1922, **94B**, 151-162.

The only reagents found to induce melanophore contraction apart from caffeine, were adrenalin, tyramine, ergotoxine and cocaine. In addition to pituitary extract apocodine and nicotine in quantities more than adequate to produce general motor paralysis gave melanophore expansion. There is no direct evidence to show a nervous control of pigment responses in Amphibia. It is suggested that possibly the synchronous color changes of Amphibia in response to normal environmental stimuli are governed by endocrine influences.—G. E. B.

The relation of the ADRENALS to the circulation. Hoskins (R. G.), *Physiol. Reviews (Balt.)*, 1922, **2**, 343-360.

From a review of the literature it is concluded that the adrenal glands have a definite pharmacologic relation to the circulation by virtue of their production of adrenin. Adrenin causes stimulation of the heart, vasoconstriction in the splanchnic and cutaneous regions and dilatation in the skeletal muscle. Increased or decreased blood pressure may result, depending upon dosage and various accessory factors. Adrenal extirpation with its resulting circulatory collapse is not entirely, if at all, due to adrenin lack, since it cannot be long forestalled by administration of the drug and it does not ensue when adrenin secretion is reduced below detectable limits. The slow development of the symptoms of epinephrectomy also indicates that they are not due to sudden failure of adrenin as a stimulatory substance. Direct experimentation shows that adrenin often depresses sympathetic irritability. Marked symptomatology develops while the sympathetic system responds well to stimulation. If adrenin deficiency is a factor, it probably operates in the effector rather than the conductor mechanisms. The adrenals are stimulated to secretion by splanchnic nerve irritation, hence are supposedly under central control. Evidence of the existence of an adrenal center immediately caudad to the corpora quadrigemina has been reported. The preponderance of the evidence indicates that adrenal depression is evoked by stimulation of the vagus or depressor nerves and augmentation by asphyxia, pain and emotional excitement. This augmentation results in a mass shifting of the blood from the skin and viscera to the organs involved in neuromuscular

exertion. The cortex is probably the indispensable part of the adrenal. The medulla apparently serves merely to reinforce the sympathetic system in times of stress.—Author's Abst.

The rôle of ADRENALIN in the hypertensive effects produced by excitation of the splanchnics or by bulbar puncture (*Papel de la adrenalina en los efectos hipertensivos producidos por la excitación del nervio esplácnico o por picadura bulbar*). Houssay (B. A.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1922, 35, 329-332.

See *Endocrin.*, 7, 104.

Comparative importance of medullary and cortical parts of the ADRENALS (*Importancia comparada de la medula y corteza de la suprarrenal*). Houssay (B. A.) & Lewis (J. T.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1921, 34, 254 (*Sec. Soc. de Biol.*).

See *Endocrin.*, 6, 417.

The ADRENALS and pancreatic DIABETES (*Suprarrenales y diabetes pancreatica*). Houssay (B. A.) & Lewis (J. T.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1921, 34, 261-265 (*Sec. Soc. de Biol.*).

Ablation of the pancreas produces diabetes in dogs deprived of the right adrenal and the medulla of the left adrenal, consequently without adrenalin.—B. A. H.

The functions of dogs deprived of the ADRENAL medulla (*Las funciones de los perros privados de la médula suprarrenal*). Houssay (B. A.) & Lewis (J. T.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1922, 35, 129-137.

See *Endocrin.*, 7, 91.

The rôle of ADRENALIN in the hypertension produced by exciting the splanchnic nerve (*Nuevas comprobaciones sobre el papel de la adrenalina en la hipertensión producida al excitar el nervio esplácnico mayor*). Houssay (B. A.) & Marconi (A. P.), *Rev. d. cir. méd. argent. y centro estud. de med.*, 1922; abst., *Rev. Sud-Am. (Buenos Aires)*, 1923, 6, 70.

See *Endocrin.*, 7, 456.

The influence of ADRENALIN on the formation of antibodies (*Die Wirkung des Adrenalins auf die Antikörperbildung*). Hrma (J.), *Casop. lék. česk. (Prague)*, 1922, 61, 1217.

Hрма injected intravenously 0.05 mg. adrenin per kg. body weight into 5 rabbits. Neither increased nor decreased formation of a hemolytic amboceptor within the serum was observed. Rabbits were treated with adrenin (method of Hayashi) and the bactericidity against bacillus anthracis was noted. The bactericidity of the serum of such animals seemed somewhat but not importantly decreased. Only one of the several animals treated showed an

increase of agglutination titer. Adrenin had no influence upon the complement. There was no experimental proof that adrenin affected the production of the antibodies in the blood serum.—A. B.

(ADRENALIN) Technique of investigating local cutaneous vasomotor reactions (*Technique de la recherche des réactions vasomotrices cutanées locales*). Juster (E.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1329-1331.

Observation of the reaction of cutaneous nerves is equivalent to examining the sympathetic system of the region under examination. One method of doing this is to inject adrenalin intradermally. One cubic milligram of a 1/1000 solution causes a central white zone of anemia with "goose flesh," the width of a franc piece, surrounded at the periphery by a red zone one-half centimeter in width. It disappears in an hour and a half. Pilocarpin gives a similar reaction. Other methods of testing are described.—T. C. B.

On the concentration of the blood and the effect of histamine in ADRENAL insufficiency. Kellaway (C. H.) & Cowell (S. J.), *J. Physiol. (Lond.)*, 1922, **57**, 82-99.

The experiments described were to determine the parts played by the adrenal cortex and medulla respectively, in causing the concentration of blood and increased susceptibility to histamine found to accompany acute adrenal insufficiency. Adult cats were used, and the adrenal medulla was destroyed by radium emanations introduced into the medulla in closed capillary tubes. To determine the amount of medulla remaining at different periods during life, the paradoxical pupil reaction to anoxemia and histamine was used. The results show that histamine causes increased output of adrenalin by a direct effect upon the adrenals. The concentration of blood in animals dying of adrenal insufficiency is due to cortical defect. The altered concentration reaction to small doses of histamine is due to medullary effect. The subcutaneous injection of adrenalin antagonizes the action of histamine in causing concentration of the blood, and masks the hypersensitiveness to histamine.
—T. C. B.

ADRENAL tumors of horses and cattle. Kimura (T.), *Sei-I-Kwai M. J. (Tokyo)*, 1921, **40**, 3-8; abst., *Arch. méd. belges (Brux.)*, 1923, **76**, 266.

Adenoma of the ADRENAL (Adenom der Nebennieren). Krecke, *München. med. Wchnschr.*, 1922, **69**, 1098.

A short note. The case is reported of a woman who had vomiting spells for 7 years. There was slight brown pigmentation of the skin. The patient had a masculine appearance and had a beard, although she had normal female sexual organs. During her dis-

ease she menstruated only once. Postmortem examination disclosed adenoma of an adrenal, not touching the kidney.—J. K.

Curves of action of levorotatory and racemic synthetic ADRENALIN (*Courbes d'action des adrénalines levogyre et racémique de synthèse*). Launoy (L.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 848-852.

ADRENALIN in nephritis (A propos des escarres adrénaliques). Lavenant, *Soc. de méd. de Par.*, 1922, Oct. 28; abst., *Presse méd. (Par.)*, 1922, 30, 980.

The author observed that he could not give even a small dose of adrenalin to subjects with nephritis who were free from urinary albumen and who possessed peripheral vasoconstriction.—R. G. H.

The ADRENALS and morphin intoxication (Suprarrenales e intoxicacion morfínica). Lewis (J. T.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1921, 34, 266-268 (*Sec. Soc. de Biol.*).

See *Endocrin.*, 6, 418.

Susceptibility of ADRENALECTOMIZED rats to toxins (Sensibilidad de las ratas suprarrenoprivas a los tóxicos). Lewis (J. T.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1921, 35, 131-133 (*Sec. Soc. de Biol.*).

See *Endocrin.*, 6, 282.

The problem of the ADRENALS (Das Nebennierenproblem). Lichtwitz (L.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 2245-2249.

Few absolute facts are known as to the function of the adrenal glands. The author gives a critical discussion of some of the fantastic theories held by many writers.—J. K.

Does the reaction to ADRENALIN obey Weber's law? Lyon (D. M.), *J. Pharmacol. & Exper. Therap. (Balt.)*, 1923, 21, 229-235.

In decerebrated cats the vascular response to repeated equal intravenous doses of adrenalin chloride is constant only when the resting level of the blood pressure at the time of injection remains the same. When the amount of adrenalin injected is increased arithmetically the blood pressure responses do not follow in proportion but bear a logarithmic relationship to the stimulus, obeying the Weber-Fechner Law.—G. E. B.

(ADRENALS) Implantation of nerves in suprarenal capsules. Maragliano (D.), *Riforma med. (Napoli)*, 1922, 38, 1133-1136 (November 27).

Since free transplants of suprarenal capsules are absorbed in a few weeks, Maragliano tried to prevent it by implantation of splanchnic or spinal nerves into the organ. Yet the nerves did not proliferate, if he left the capsules in place, nor if he transplanted them

with the nerve. The absorption of the transplanted capsule was not prevented by this proceeding.—J. Am. M. Ass., 80, 285.

Hypofunction of the ADRENAL glands and rachitis. Massaglia (A. C.), J.-Lancet (Minneap.), 1922, 42, 301-306.

A preliminary report suggesting that experimental adrenal deficiency in pregnant animals may give rise to rachitic changes.

—R. G. H.

The weight of the ADRENALS (Das Gewicht der Nebennieren). Materna (A.), Ztschr. f. Konstit. (Berl.), 1923, 9, 1-5.

The combined weight is given of the 2 adrenals of 25 normal adults (21 males and 4 females, 19 to 68 years of age) with accidental sudden death. Most of the males were young adults. The weight of the 2 glands varied from 5.15 to 13 gms., most of them being below 10 gms.; this is somewhat lower than is reported by the literature, as indicated by a table giving the weights obtained by others in over 1000 cases. Some references are given.—A. T. R.

Intracardial injection of ADRENALIN and subcutaneous injection of lobelin in asphyxia pallida of the new born child (Intrakardiale Adrenalininjektion und subkutane Lobelininjektion zur Bekämpfung der Asphyxia pallida des Neugeborenen). Mikulicz-Radecki (F.), Zentralbl. f. Gynäk. (Leipz.), 1922, 46, 1574-1579.

Intracardial injection of 0.5 mg. of suprarenin, combined with a subcutaneous injection of 3 mg. of lobelin, gave splendid results.

—J. K.

Sull' ADRENALINA. Milliam, Chim. e med. mod. (Milano), 1922, 2, 10-15.

The OVARY and ADRENALINE hyperglycosuria. Mochizuki (K.), J. Jap. Gyn. Soc., 1921, 16, No. 9; Jap. Med. World, 1922, 2, 46.

The injection of adrenaline causes a more marked hyperglycosuria after experimental oöphorectomy, atrophy of the ovary in the menopause, or functional derangement of the ovaries by x-rays.

—Physiol. Abst., 7, 555.

Experimental studies on the SUPRARENAL cortex. Mori (S.), Nihon Biseibutsugakukai Zasshi (Kyoto), 1923, 17, 227-265.

In the rabbits fed with fats, chemical and histological changes in the suprarenal cortex were looked for. The cortex, especially the zona reticularis and striata, was enlarged, and the amount of neutral fats and cholesterin ester was increased, while cholesterin and other lipoids were present in small amounts. Lipemia and cholesterinemia were also found in accordance with their amounts contained in the suprarenal. Hence the suprarenal seems to be an organ related to the metabolism of neutral fat and cholesterin. The above changes were never found in the suprarenal medulla.—S. K.

Studies on ADRENALIN discharge. Morita (M.), Fukuoka Ikadai-gaku Zasshi (Fukuoka), 1923, 16, 1-59.

The author determined the adrenalin content in the suprarenal of dogs, rabbits, and guinea-pigs under various conditions. If the blood pressure was lowered by nitrites or toxins, the adrenalin content was lowered, owing to its increased discharge. This fact did not appear after cutting the sympathetic nerve. A decrease of the adrenalin content was also found after electrical stimulation of the splanchnic nerve. Degenerative atrophy and fibroid degeneration were found not only in the medulla but also in the cortex after cutting the sympathetic. The author thinks that in experiments on the suprarenal cutting of the postganglionic fibres to the gland is preferable to that of the splanchnic nerve since the vasodilatation of its area may be avoided. The increase of the adrenalin discharge caused by a fall of the blood pressure may be prevented by an intraperitoneal injection of adrenalin, although it has no such effect if injected intravenously or subcutaneously. In Weil's disease the adrenalin content in the suprarenal diminishes remarkably, and it has been proved by experiments on 26 patients that the intraperitoneal injection of adrenalin acts very beneficially.—S. K.

Action of ADRENALIN on the curve of hyperglycemia (*Influencia de la adrenalina sobre la curva hipercalcémica provocada*). Muñoz (J. M.), Rev. Asoc. méd. argent. (Buenos Aires), 1921, 34, 166-172 (Sec. Soc. de Biol.).

See Endocrin., 6, 282.

The ADRENALIN content in the SUPRARENAL of the tuberculinized guinea-pigs. Nakada (K.), Kekkaku (Tokyo), 1923, 1, 50-64.

Tubercle bacilli were injected into guinea-pigs, subcutaneously, intravenously or into the abdomen. After several days the pigs were killed and the adrenalin content in the suprarenal was determined by Sudo and Inouye's method. A diminution was found in most cases, especially in the late stages and in the severe cases of the disease. The same was also found after tuberculin injection.

—S. K.

Action of ADRENALIN and of suprarenal extract on muscular excitability (*Action de l'adrénaline et de l'extrait surrénal sur l'excitabilité musculaire*). Obré (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 585-588.

A typical myasthenia gravis pseudoparalytica, combined with scleroderma and weakness of the ADRENAL system (*Eine atypische Form der Myasthenia gravis pseudoparalytica kombiniert mit Sklerodermie und Schwäche des Adrenalsystems*). Patrzek (F.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.), 1921, 63, 155-162; abst., Schweiz. med. Wchnschr. (Basel), 1922, 52, 1238.

On the basis of the characteristic microscopic picture in a bit of excised muscle the diagnosis of myasthenia gravis was made in a 30 year old woman. The case was atypical in that the ordinary electric reaction was lacking, as was atrophy of the shoulder girdle and quick fatigability. Death occurred, as is usual, from respiratory failure. At autopsy marked changes were found in the diaphragm and intercostal muscles. Scleroderma was present in the face, hands and feet; this first appeared about two years before the myasthenia symptoms. The author believes that the "adrenal system" was weak because the patient showed pigmentation of the face (but not of the mucosa of the mouth and throat), lowered blood pressure and hypoglycemia; the latter two symptoms were not influenced by adrenalin injection. At autopsy the adrenals as well as the other endocrine glands were found intact. The author believes that the findings as a whole indicated an endocrine etiology.

—R. G. H.

(ADRENALS) Addison's disease. Peiper (H.), *Ztschr. f. Urol.* (Leipz.), 1923, 17, 40-50.

Peiper recommends roentgen-ray examination of the kidney region after insufflation of oxygen into the bed of the kidney. He advocates removal when the suprarenal capsule is the seat of a unilateral tuberculous process.—*J. Am. M. Ass.*, 80, 1350.

Disturbed formation of adrenalin in the ADRENALS due to external causes, and its biological significance (*Störungen der Adrenalinbildung in den Nebennieren unter äusseren Einflüssen und ihre biologische Bedeutung*). Peiser (B.), *Ztschr. f. d. ges. exper. Med.* (Berl.), 1922, 28, 234-264.

See *Endocrin.*, 6, 667.

(ADRENALS) Vitiligo in subjects with Addison's disease (*Le vitiligo chez les addisoniens*). Piéri (J.), *Thèses de Par.*, 1922; abst., *Presse méd.* (Par.), 1922, 30, 940.

Vitiligo is seen in diseases of the incretory glands, whether these affections are due to syphilis or not, particularly in certain cases of Addison's disease. This relationship gives the melanoderma a particular aspect characterized by the presence of three tones of coloring and a symmetrical topography. Diagnosis is easy. In vitiligo, as in the melanoderma of Addison's disease, the pigmentary disorders are sometimes accompanied by a trophic disturbance involving scleroderma. To explain the pathogenesis of vitiligo the author supposes that it is through the sympathetic system that pigmentation is caused to reappear to the surface of the skin; disturbance of this function by irritation of near-by ganglia and nerve fibers or by endocrine disorders is the determining factor in the pigmentation seen in Addison's disease.—R. G. H.

The action of **ADRENALIN** (*Über die Wirkung des Adrenaline*).
Platz (O.), *Klin. Wchnschr.* (Berl.), 1922, 1, 1895-1896.

Intravenous injection of adrenalin nearly always first raised then lowered the blood pressure. When the blood pressure was first increased, 0.005 mg. would produce a marked reaction; in many persons even 0.001 mg. was enough to produce a change of blood pressure. When given subcutaneously the minimum active dose was 0.1 mg. When atropine or papaverin were given together with adrenalin the rise of blood pressure was much higher than after injection of adrenalin alone. After intravenous injection of adrenalin 94% showed an increased pulse rate; 6% a lowered one. No case was noted in which the pulse rate remained unaltered. The same was seen after subcutaneous injection. Respiration became more frequent in 80% of the subjects and less in 20% after intravenous administration. Blood sugar was always increased, but glycosuria was seen only when adrenalin was administered subcutaneously and then only in 4% of the cases. Intravenous injection caused a rise of the NaCl in the blood; the influence of subcutaneous injections was not studied. The number of red and white corpuscles was increased by both means of administration. The number of neutrophil cells usually became smaller, especially after intravenous injection. In several cases a diminished number of eosinophil cells was seen, but no general rule could be formulated concerning them. Rectal administration of adrenalin was absolutely inactive and the custom of adding adrenalin to enemas must therefore be considered as useless.—J. K.

The action of **ADRENALIN** on the pneumococcus (*Recherches expérimentales sur l'action de l'adrénaline sur le pneumocoque*).
Puscariu (E.) & Nitzulescu (I.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 540-541.

Experiments with **ADRENALIN** (*Weitere Versuche über Adrenalin*).
Proebsting, *Klin. Wchnschr.* (Berl.), 1922, 1, 2018.

The author describes a colorimetric method of finding adrenalin in a solution of 1:100 millions. The biological method enables us to detect still smaller quantities. When the posterior part of a frog is sensitized by perfusion of a solution of adrenalin for a long period it shows reaction when a solution of 1:½ milliard of adrenalin is added. If possible, therefore, this reaction is preferred.—J. K.

Glycemic reaction to the intramuscular administration of **EPI-NEPHRIN**. Raphael (T.) & Parsons (J. P.), *Arch. Neurol. & Psychiat.* (Chicago), 1922, 8, 172-178.

Blood sugar determinations were made after the intramuscular injection of .1 mg. of epinephrin in 3 normal subjects, 9 cases of dementia praecox and 6 of manic depressive insanity; of the latter,

3 were in the excited phase and 3 of the depressive type. In the normal persons the blood sugar curve reached its maximum in from 30 minutes to 1 hour with subsidence in $3\frac{1}{2}$ hours. The reaction pit or point of minimal glycemia is definitely below the initial fasting level following which there is a definite rebound to approximately this level. In the psychotic subjects the general contour is essentially the same as in normal persons for the first $3\frac{1}{2}$ hours, following which, however, the depressed and dementia praecox subjects become variant in that a further gradual drop is noted with slight or no indication of rebound, a deviation which conceivably may be of basic metabolic import.—C. E. N.

Effects of repeated transplantation of whole SUPRARENALS into young doves. Riddle (O.) & Minoura (T.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, **20**, 456-461.

The adrenal tissue from other doves was placed subcutaneously and repeated grafts were made since the transplants were gradually resorbed. When compared with the controls the experimental birds showed clearly an earlier sexual maturity in the female, as indicated by the appearance of the first egg. An enlargement of the testes, a reduction in the size of the ovaries, and a retardation of sexual maturity in the male also occurred, but the authors do not feel that their evidence is conclusive on these points. The descendants of the experimental birds were normal in every way.—J. C. D.

Changes in EPINEPHRIN secretion during cerebral anemia. Rogoff (J. M.), *J. Pharmacol. & Exper. Therap.* (Balt.), 1923, **21**, 211-212.

A study of the rate of epinephrin secretion during and following the production of cerebral anemia in the cat. Blood was taken from the adrenal vein and assayed on rabbit intestine segments. Definite increases (3 to 8 times the initial rate) were shown in the output during the early part of the occlusion of the head arteries. This increased rate fell to the initial rate or below after occlusion. The conclusion is made that during the period of vasomotor response in cerebral anemia the rate of epinephrin secretion may be increased, but this has no material effect on the character or the degree of the vasomotor response to the anemia brought about by the bulbar centers.—G. E. B.

Observations on the supposed relation of the ADRENAL glands to the blood-pressure response during cerebral anemia. Rogoff (J. M.) & Coombs (H. C.), *Am. J. Physiol.* (Balt.), 1923, **64**, 44-74.

There is no significant difference in the responses to occlusion of the head arteries between normal animals and those in which epinephrin secretion is interfered with. Adrenal activity is not necessary for eliciting any of the vasomotor effects resulting from acute cerebral anemia.—T. C. B.

(ADRENAL) Morbus Addisoni. Rosenow, Klin. Wchnschr. (Berl.), 1922, 1, 502.

Data reported elsewhere.—J. K.

ADRENALINEMIA. San Martin (G.), Crón. méd.-quir. de la Habana, 1922, 48, 170-172.

Behavior of the ADRENALS in experimental scaldings (Sul comportamento delle capsule surrenali nelle scottature). Salvioli (G.), Sperimentale. Arch. di biol. (Firenze), 1922, 76, 190.

Experiments were made by scalding the skin of guinea-pigs. According to the extension and severity of the scaldings, the changes of the blood circulation of the adrenals varied from a simple congestion to hemorrhages and blood coagulation. In the cells of the cortex the neutral fats, lipoids, and pigment were increased; in those of the medulla the chromaffin substance was diminished. The same results were obtained in guinea-pigs in which one adrenal had been previously removed.

—Med. Sc., 8, 232.

Changes of arterial pressure following subcutaneous injection of ADRENALIN and its significance [Variazioni della pressione arteriosa indotte dall' iniezione sottocutanea di adrenalina e loro significato. (Nota preventiva)]. Sanguinetti (A.), Malatt. d. cuore, 1921, 5, 93-99; abst., Ber. ü. d. ges. Physiol. (Berl.), 1922, 12, 265.

The author believes that the individual differences in adrenalin effect are due to the slowness of absorption. It was observed that 4 vagotonics reacted with a rise in blood pressure and an immediate and decided bradycardia, while 4 others showed tachycardia before the slowing of the pulse. This symptom may be of some diagnostic value also.—R. G. H.

(ADRENALS) Combination of scleroderma with Addison's disease, with Raynaud's disease and with tendovaginitis crepitans (Kombination von Sklerodermie mit Addisonscher Erkrankung; Kombination von Sklerodermie mit Raynaudscher Krankheit und Tendovaginitis crepitans). Scholz (K.), Klin. Wchnschr. (Berl.), 1922, 1, 1948-1949.

The author observed a man of 41 with scleroderma. The thyroid was small. Ingestion of 100 gm. of glucose did not cause glycosuria. The author believed this to be a complication of Addison's disease with scleroderma. The body was darkly pigmented, but the mucous membranes did not show any special color. Blood pressure was 106 mm. Blood sugar determinations are not given. The other cases reported are not of endocrine interest.—J. K.

Origin of tuberculosis of the ADRENAL glands. Schwarz (F.), *Ztschr. f. Tuberk. (Leipz.)*, 1922, **37**, 169-184; *ibid.*, 1923, No. 4 (Jan.); *abst., Presse méd. (Par.)*, 1923, **31**, 108.

Schwarz reports 20 cases of tuberculosis in which the adrenal glands were examined anatomically and histologically; 14 of the subjects were children of 3 months to 6 years; the 6 others were adults of 18 to 64 years. In 17 cases there was general miliary tuberculosis and in 14 of these, that is 83%, there existed miliary tuberculosis of the adrenal glands. It was concluded, therefore, that in general miliary tuberculosis the adrenals are frequently involved. Schwarz noted that the right adrenal was more often affected than the left. Miliary tuberculosis seems to have a different effect in the cortex and in the medulla. Two forms are observed: one is characterized by uniform caseation, while the other shows epithelioid and giant cells. Between the two there is a transitory phase. Usually, the older the subject, the more numerous the giant cells. The tuberculous bacilli are more abundant in the uniformly caseous points. Histologically, lesions of the adrenals in miliary tuberculosis correspond to changes genetically analogous to other organs (spleen, liver, kidney, lungs). The chronic tuberculosis of the adrenal glands, of which the author found 65 cases in 19,061 autopsies assembled from January 1, 1904, to May 30, 1922, was always secondary. Chronic tuberculosis of the adrenals is seen more rarely than miliary.—R. G. H.

The blood picture after ADRENALIN injection. Shimizu (J.), *Hokuetsu Igakukai Zasshi (Nigata)*, 1922, **37**, 692-731.

In blood from the ear-lobe of patients, and in that taken from the mesenteric or the splenic vein of rabbits, the number of the leucocytes was increased after the injection of adrenalin. This increase was found in all leucocytes, but was especially prominent in the lymphocytes. Such increase was also largely confirmed in splenectomized rabbits. Opposite results were obtained in the blood taken from the mesenteric vein. Hence the cause of the increase is probably not attributable only to a contraction of the spleen produced by adrenalin, but also to changes in the distribution of leucocytes in the blood vessels.—S. K.

(ADRENIN) Influence of ischaemia on infection. Sollmann (T.) & Brody (J. G.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1922, **19**, 400-401.

The authors show that if one ear of a rabbit is rendered bloodless by injecting adrenin and then both ears are wounded and the wounds infected the injected ear will be much less resistant to the infection and will recover much more slowly than the uninjected ear.

—J. C. D.

The supposed relation of the ADRENALS to reflex volume changes in the denervated limb. Stewart (G. N.) & Rogoff (J. M.), *Am. J. Physiol. (Balt.)*, 1923, 63, 436-478.

It is said that the constriction of the denervated limb following (passive) dilatation, elicited by stimulation of the central end of the sciatic, which some observers think evidence of increased output of epinephrin, has no such significance. The reaction can be obtained when the glands have been eliminated.—T. C. B.

The blood changes and their relation to the spleen, which are caused by pilocarpin, atropin and ADRENALIN. Takaori (S.), *Chugwai Iji-Shimpo*, 1922, No. 1019; No. 1020 (September); cit., *Jap. Med. World (Tokyo)*, 1922, 2, 347.

Morphology of the ADRENAL glands. Takeya (O.), *Kyoto Igak-kwai Zasshi*, 1922, 19, No. 3 (April); cit., *Jap. Med. World (Tokyo)*, 1922, 2, 263.

The influence of vaccines on ADRENALIN discharge. Tokumitsu (M.), *Igakuchuo Zasshi (Tokyo)*, 1923, 20, 1363-1373.

The author determined the adrenalin content of the blood and of the suprarenal of rabbits after an injection of some vaccines. About 30 to 90 minutes after the injection, the adrenalin discharge was increased, while its amount varied with the sort of vaccines. Carboxyl acids and normal horses' serum had no influence on the adrenalin discharge. These results were not altered by cutting the sympathetics, demonstrating that this action of vaccines is not central, but peripheral in origin.—S. K.

The alterations of the organs, owing to the disappearance or the diminution of the function of the SUPRARENAL body, especially on the relation of the suprarenal cortex to thyroid. Tokumitsu (M.), *Tohoku Igakukai Zasshi (Sendai)*, 1922, 6, 85-102.

Gradual destruction of the adrenals of rats was succeeded by transplantation of Flexner's (rat) cancer beneath the capsule of this body. At different times in the course of destruction, histological variations in the thyroid and pituitary body, etc., were examined. A parenchymatous goitre was found when the function of the suprarenal cortex was entirely, or seriously disturbed, but a colloid goitre if this disturbance was slight, the destruction of the medulla being without influence in any case. Variations in histological types of goitre may therefore result from degrees of variations in the suprarenal cortex, that is, a slight destruction of the latter causes the thyroid to become charged with more abundant colloid material, and a serious one causes a multiplication of the epithelial cells. In one case of moderate destruction, a mixed type of these two variations was found. If the function of the suprarenal body was entirely destroyed, the principal cells of the pituitary

multiplied and became dark, while if the function of the suprarenal cortex was maintained to some extent, the multiplied cells were not so dark. Atrophy and diminution of the eosinophile cells were found with a serious destruction of the suprarenal medulla, but this was not the case if the medulla was in normal condition, even when the cortex was completely destroyed.—S. K.

The influence of the immune serums upon ADRENALIN discharge.

Tokumitsu (M.), Igakuchuo Zasshi (Tokyo), 1923, 20, 1450-1460.

The immune serums excite adrenalin discharge. This action may be attributed to the immune bodies contained in the serums, because normal horses' serum has no such action. In almost all cases this action is peripheral in origin. The adrenalin discharge was more pronounced if the serum used was warmed up to 80-100° C.—S. K.

Influence of ADRENAL cortex preparations as well as other endocrine organs on the adrenalin secretion. Tokumitsu (B.), Tokyo Iji-Shinshi, 1922, Nos. 2291, 2292 (August).

The cortical layer preparation not only inhibits adrenalin secretion, but also produces a substance that neutralizes adrenalin. The infusion itself has vasodilator action. Normal and Basedow's thyroid facilitates adrenalin secretion, but this action does not manifest itself if the visceral sympathetic nerves have been severed. By cutting the vagus nerves, adrenalin secretion is suspended for about a quarter of an hour. The cortical layer of the suprarenal capsules counteracts the thyroid. Infusion of spleen inhibits adrenalin secretion and has a vasodilator action. Infusion of the posterior lobe of the pituitary body inhibits adrenalin secretion, but that of the anterior lobe enhances the secretion, while both have vasodilator action. The pineal body and the corpus luteum enhance the secretion, but the thymus has no effect.—Jap. Med. World, 2, 345.

Reality of HYPERADRENALINEMIA due to excitation of the splanchnic nerve. Reply to Zunz and Govaerts (*Réalité de l'hyperadrénalinémie par excitation du nerf splanchnic. Réponse à MM. Zunz et Govaerts*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1159-1161.

A reply to their critics, maintaining the correctness of their previous findings.—T. C. B.

Determination of the quantity of ADRENALIN secreted by the suprarenal during excitation of the splanchnic; calculation of the amount of hyperadrenalemia thus created (*Détermination de la quantité d'adrénaline secrétée par la capsule surrénale pendant l'excitation du splanchnique; calcul de taux de l'hyperadrénalinémie ainsi créée*). Tournade (A.) & Chabrol (M.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 6-7.—T. C. B.

Optimum conditions of absorption of ADRENALIN by the digestive tract (Conditions optima d'absorption de l'adrénaline par voie digestive). Trias (A.) & Dorlencourt (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1189-1190.

The authors have shown that adrenalin is absorbed from the digestive tract, as evidenced by the hyperglycemia produced after it has been introduced into the stomach. By reason of its therapeutic value they have sought for the conditions which favor its absorption. It is found that the more concentrated the solution the more readily it is absorbed, but the maximum hyperglycemia is delayed. Also rendering it isotonic by Ringer's solution favors absorption.

—T. C. B.

Lesions of the ADRENAL capsule in a case of sudden death of a new-born (Lésions de la capsule surrénale dans un cas de mort subite chez un nouveau-né). Vallois & Roume, *Bull. Soc. d'obst. et de gynéc. (Par.)*, 1923, 12, 82-83; see also, *Gynéc. (Par.)*, 1923, 22, 175.

The ADRENAL glands in their relation to modern medicine. Weiler (R.), *Am. J. Clin. M. (Chicago)*, 1921, 28, 544-548, 618-623, 697-704.

A general review of the anatomy, physiology, embryology, and chemistry of the adrenal gland with a summary of its principal clinical aspects. Nothing new.—A. T. R.

(ADRENIN) Observations on substances which increase the excitability of the vomiting centre. Weiss (S.) & Hatcher (R. A.), *J. Pharmacol. & Exper. Therap. (Balt)*, 1923, 21, 220.

The excitability of the vomiting centre in cats and dogs was tested by the local application of small amounts of many drugs including epinephrin. In quantities of 0.01 mg. per kilogram weight epinephrin produced emesis.—G. E. B.

The ADRENALS of tuberculous patients (Die Nebennieren tuberkulöser Individuen). Wiesner, *Wien. klin. Wchnschr.*, 1923, 36, 352-353.

In the adrenals of patients with tuberculosis changes may occur showing regenerative processes with degeneration of the cortex, but without real development of tubercles. The author considers these changes as of "tuberculotoxic" origin.—J. K.

Diseased conditions in a case of disturbed tonus of the AUTONOMIC NERVOUS SYSTEM (Les états de déviation du tonus des systèmes nerveux de la vie organo-végétative). Guillaume (A. C.), *Bull. méd. (Par.)*, 1922, 36, 200-207; *abst., Ber. ü. d. ges. Physiol. (Berl.)*, 1922, 14, 48.

After studying the observations made by Eppinger and Hess on the diseased state of the body following vagotonia, and keeping

in mind the pharmacological symptoms of the autonomic nervous system, the author gives a systematic survey of the pathological conditions which accompany the disturbance of equilibrium of this system. From the possible combinations of hyper- and hypotonia of the sympathetic and parasympathetic systems, the most important conditions from a practical point of view are hypertonia of the sympathetic on one hand, and sympathetic hypotonia and vagotonia on the other. These conditions the author describes in great detail with especial regard to their symptomatology and etiology. Among other things, incretory disturbances are discussed. Critical considerations of the diagnostic methods and therapeutic measures are also included.—R. G. H.

Studies on blood lipoids. The relation of cholesterol and protein deficiency to BASAL METABOLISM. Epstein (A. A.) & Lande (H.), Arch. Int. Med. (Chicago), 1922, 30, 563-577.

The author believes that a definite relationship exists between the blood cholesterol and diseases of the suprarenal and thyroid. The normal value for cholesterol in the blood ranges between 160 and 200 mg. per 100 cc. The Bloor modification of the Funk-Antenrieth method was used. A low blood cholesterol value was found in cases with increased basal metabolism and a high blood cholesterol content in those with lowered basal metabolism, especially those with edema or myxedema. The authors believe that the blood cholesterol is an index of the lipid content of the suprarenal cortex and body tissue. In nephrosis, basal metabolism determinations were found very valuable in differentiating cases suitable for high protein and thyroid therapy. The remarkable improvement in these cases under thyroid extract is explained by its promoting the utilization of protein, thus ultimately influencing the edema.—H. L.

Study in BASAL METABOLISM in dementia praecox and manic-depressive psychosis. Gibbs (C. E.) & Lemcke (D.), Arch. Int. Med. (Chicago), 1923, 31, 102-115.

Fifteen cases formed the manic group and eleven cases belonged in the dementia praecox group. Basal metabolic determinations were made, all possible experimental precautions being taken. Definitely abnormal rates were found in psychotic patients in the more acute phases of their psychosis. The variations from normal were greater in dementia praecox patients than in manic-depressive insanity. The patients did not show sufficient evidence to explain satisfactorily the findings in terms of thyroid or pituitary disorders. Several of the dementia praecox patients did show some evidence of disturbed growth, including incomplete sex maturity. Thyroid extract by mouth raised the rate to normal in two cases, but no immediate mental improvement took place. Inanition was not

thought to account for the readings except possibly to some extent in two cases.—H. L.

Chemical studies on the relation of the CAROTID GLAND to the ADRENAL system (Chemisches über die Zugehörigkeit der Carotisdrüsen zu dem Adrenalsystem). Aszódi (Z.) & Paunz (L.), *Biochem. Ztschr.* (Berl.), 1923, 130, 159-162.

Water extracts were made from the carotid glands of freshly killed horses. The possibility that these extracts might contain a substance having the properties of adrenalin was tested by qualitative chemical tests, by the action of the extracts on smooth muscle and by their effect on sugar excretion when injected into white rats. In all cases the tests were negative and the author accordingly concludes that the carotid gland is not a member of the adrenal system.

—F. S. H.

Tumors of the CAROTID gland (I tumori della glandola carotica). Fedeli (F.), *Arch. ital. di chir.*, 1922, 6, 217; abst., *Med. Sc.* (Lond), 1923, 8, 31.

Detailed report on an individual tumor and a review of the literature.—R. G. H.

The action of PANCREATIC extract in DIABETES (A propos de l'action de l'extrait pancréatique dans le diabète). Achard, *Acad. de méd. (Par.)*, 1923, April 3; abst., *Presse méd. (Par.)*, 1923, 31, 327.

(DIABETES) Uber Urobilin. Adler (A.), *Deutsches Arch. f. klin. Med.* (Leipz.), 1922, 140, 302-322.

Urobilin is a normal substance in human urine, about 20 to 25 mg. being excreted daily in health. Administration of sugar in diabetes causes an increased amount of urobilin. In light cases of diabetes it is not excreted in abnormal quantities, but the more severe the case the greater the amount of urobilin excreted. Injection of adrenin causes marked augmentation of the high urobilin excretion seen in hemolytic jaundice.—J. K.

A rapid method of preparing the ANTI-DIABETIC substance of pancreas. Allen (R. S.), Kimbell (C. P.) & Murlin (J. R.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 519-521.

Dietetic treatment of DIABETES MELLITUS (Neuere Gesichtspunkte in der Diätbehandlung des Diabetes mellitus). Assmann, *Munchen. med. Wehnschr.*, 1922, 69, 1323.

See *Endocrin.*, 7, 461.

INSULIN. Banting (F. G.), *Michigan State M. Soc. J.* (Grand Rapids), 1923, 22, 113-124; cit., *J. Am. M. Ass.* (Chicago), 1923, 80, 1341.

The effect produced on **DIABETES** by extracts of pancreas. Banting (F. G.), Best (C. H.), Fletcher (A. A.), Macleod (J. J. R.) & Noble (E. C.), Tr. Ass. Am. Physicians (Phila.), 1922, **37**, 337-347.

A report of progress.—I. B.

Clinical experience with insulin (**PANCREATIC** extracts) in treatment of **DIABETES MELLITUS**. Banting (F. G.), Campbell (W. R.) & Fletcher (A. A.), J. Trop. M. [etc.] (Lond.), 1923, **26**, 50-54; cit., J. Am. M. Ass. (Chicago), 1923, **80**, 961.

Anatomo-pathologic and pathogenetic study of **DIABETIC** retinitis (*La rétinite diabétique—étude anatomo-pathologique et pathogénique*). Beauvieux & Pesme (P.), Arch. d'opht. (Par.), 1923, **40**, No. 2 (Feb.); abst., Presse méd. (Par.), 1923, **31**, Analyse 16 (April 7).

Impending and real gangrene associated with **DIABETES**. Correlation of medical and surgical effort. Bernheim (B. M.), Am. J. M. Sc. (Phila.), 1922, **163**, 625-634.

Bernheim, of the Surgical Clinic of the Hebrew Hospital, Baltimore, records 3 cases illustrating the importance of correlation between the physician and surgeon in the treatment of impending and actual diabetic gangrene.—Med. Sc., **7**, 363.

Treatment of **DIABETES** with **INSULIN**. Blum. (L.), Bull. Acad. de méd. (Par.), 1923, **88**, 73.

Blum prepared insulin according to Banting and Best's method, and reports two favorable clinical experiences. In the debate, Achard mentioned similar organotherapeutic experiments at his school in 1919, and especially some experiments, never published, which his pupil Gardin made with decoctions of pancreas. The transient suppression of glycosuria, valuable as it is, is not a cure for diabetes. Gley mentioned also his experiments. He did not use ligation of ducts, because they regenerate too easily. He injected fats into the ducts, and stained them to see whether the whole pancreas was injected. He deplores the lack of facilities for keeping animals for experimental work, which prevents many researches in France.—J. Am. M. Ass., **80**, 963.

The influence of **INSULIN** on the curve of glycemia in **DIABETES** (*L'influence de l'insuline sur la courbe de la glycémie dans le diabète*). Blum (L.) & Schwab (H.), Compt. rend. Soc. de biol. (Par.), 1923, **88**, 463-464.

Treatment of **DIABETES** by **INSULIN** (*Traitement du diabète par l'insuline*). Blum (L.) & Schwab (H.), Soc. de méd. du Bas-Rhin, 1923, Jan. 27; abst., Presse méd. (Par.), 1923, **31**, 184.

One subject who had been in diabetic coma for 2 hours was notably improved after 3 doses of insulin; the acid intoxication

disappeared. Another patient, intoxicated to a much greater degree, with an alkaline reserve of 0.23 and a glycemia of 4.94 gm., presented after 3 days of treatment an alkaline reserve of 0.56 and a glycemia of 1.24 gm.—R. G. H.

Lumbar puncture in DIABETES. Bordini Posse (C.), *Rev. méd. d. Uruguay* (Montevideo), 1922, 25, 858-862.

Bordini Posse adds another case to the few on record in which diabetes seemed to be favorably influenced by lumbar puncture. Lhermitte has reported subsidence of glycosuria and polyuria after lumbar puncture in 2 cases of diabetes. In Bordini Posse's case there was intense acetonuria and diaceturia, and 6 liters of urine. After lumbar puncture, without change of diet, the glycosuria dropped from 360 to 5 gm. and the polyuria to 1 liter. The acetonuria persisted, but finally subsided after an oatmeal day. The man, aged 35, left the hospital free from glycosuria and polyuria and acetonuria. The diet contained 1,900 calories and 60 gm. of carbohydrates. The sugar content of the blood was 1.15. The author suggests that lumbar puncture relieves pressure on the central nerve centers which control the sugar content of the blood.

—J. Am. M. Ass., 80, 1107.

DIABETES. Bose (J. P.), *Indian J. Med. (Calcutta)*, 1922, 3, 263-268; cit., *J. Am. M. Ass.*, (Chicago), 1923, 80, 1103.

Balancing the ration in severe DIABETES. Brown (A. G.), *Virginia M. Month. (Richmond)*, 1923, 49, 706-708; cit., *J. Am. M. Ass. (Chicago)*, 1923, 80, 1178.

DIABETES with acidosis and its treatment (*Notes sur le diabète avec acidose et son traitement*). Brunon Guardia (R.), *Normandie méd. (Rouen)*, 1922, 33, 3-6 (suppl.).

Experimental DIABETES MELLITUS (*Diabète sucré expérimental*). Camus (J.), Gournay (J. J.) & Le Grand (A.), *Compt. rend. Acad. d. sc. (Par.)*, 1923, 177, 146-148.

Experimental lesion of the tuber cinereum in rabbits produces a glycosuria of much longer duration (up to several weeks) than does Claude Bernard's puncture.—A. T. C.

Study of the acetogenic and antiacetogenic equilibrium of metabolism in the spontaneously DIABETIC dog of Maignon (*Etude de l'équilibre acétogénique et antiacétogénique dans la métabolisme de la chienne spontanément diabétique de Maignon*). Carrasco-Formiguera (R.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 611-614.

(DIABETES) Criticism of some points in the doctrine of Maignon on acetonuria (*Critique de quelques points de la doctrine de Maignon sur l'acétonurie*). Carrasco-Formiguera (R.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 614-616.

(DIABETES) The influence of various carbohydrate foods on glycemia (Influence de divers aliments hydrocarbonés sur la glycémie). Casteigts (M.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 86, 1110-1112.

(DIABETES) Influence of different carbohydrates on glycosuria (Influencia de diversos alimentos hidrocarbonados sobre la glucemia). Casteigts (M.), *Rev. Asoc. méd. argent. (Buenos Aires)*, 1922, 35, 28-41.

In diabetic and in normal subjects it was observed that with administration of equivalent amounts of carbohydrates from different sources the hyperglycemic curve became greater decreasingly after the ingestion of 75 gm. of glucose, 250 gm. rice, 450 gm. potatoes and 300 gm. oats respectively. Three hours afterwards the glycemia was less than in the beginning.—B. A. H.

Action of the alcoholic extract of PANCREAS (insulin) on critical glycemia [Action de l'extrait alcoolique de pancreas (insulin) sur la glycémie critique]. Chabanier (H.), Lebert (M.) & Lobo-Onell (C.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 480-482.

A method of preparation to be published later.—T. C. B.

The rôle of the renal threshold of glucose in the phenomenon of tolerance in DIABETICS (Du rôle du seuil rénal du glucose dans le phénomène de tolérance chez les diabétiques). Chabanier (H.), Lebert (M.) & Loro-Onell (C.), *Arch. d. mal. d. reins*, 1922, 1, 112-122; abstr., *Ber. u. d. ges. Physiol. (Berl.)*, 1923, 16, 234.

Adipsia and pain in the epigastrium as premonitory signs of DIABETIC coma (L'adipsie et l'épigastralgie, signes précurseurs du coma diabétique). Chalier (J.), *Lyon méd.*, 1922, 131, 263-266

The author, who records a case in a man aged 63, who had had diabetes for 8 years, emphasizes the importance of adipsia and pain in the epigastrium as premonitory signs of diabetic coma. Adipsia has not hitherto been mentioned as a prodromal sign of coma, whereas the significance of epigastric pain in this connection has long been known.—*Med. Sc.*, 7, 358.

Method employed for controlling DIABETICS in outpatient department of Lakeside Hospital. Christie (C. D.), *Ohio State M. J. (Columbus)*, 1923, 19, 250-253; abstr., *J. Am. M. Ass. (Chicago)*, 1923, 80, 1543.

DIABETES MELLITUS in a child of 22 months. Colburn (O.), *Arch. Pediat.*, 1922, 39, 48-51; abstr., *Med. Sc. (Lond.)*, 1923, 7, 360.

It is not frequent to find a diabetic patient producing a diabetic child, as in the case reported by Colburn in a child aged 22 months, whose father had had glycosuria for a number of years.—R. G. H.

Carbohydrate metabolism in avitaminosis (Der Kohlehydratstoffwechsel bei Avitaminose. II. Glykogen und Avitaminose). Collazo (J. A.), *Biochem. Ztschr.* (Berl.), 1923, 136, 20-25.

The liver is practically glycogen-free in the hyperglycemic state of avian avitaminosis. The same is true for dogs and guinea-pigs. In birds the body as a whole is practically glycogen-free. This holds for muscle tissue. This condition thus differs from that of simple starvation in that there the liver, heart and skeletal muscle tissue contain relatively an increased glycogen content. The three vitamins, A, B, and C play a similar role in the carbohydrate metabolism of birds and carnivora.—F. S. H.

The influence of glucose in small and large amounts on the blood-sugar of normal, fasting and avitaminotic organisms (Ueber den Einfluss von Traubenzuckerzufuhr in kleinen und grossen Mengen auf den Blutzucker beim normalen, hungernden und aviataminösen Körper). *Ibid.*, 26-37.

The avitaminotic organism differs from the normal and fasting animal (dog) in the reaction of its carbohydrate to the peroral, rectal, intraperitoneal, intravenous and subcutaneous administration of glucose. When large amounts of the sugar are given the hyperglycemia is more intense, more prolonged and glucosuria is more easily induced in the avitaminotic organism. When small doses of glucose are given the hypoglycemic stage is less though more prolonged.—F. S. H.

The toxic action of the products of intermediary metabolism after the administration of various sugars in avitaminosis (Ueber die toxische Wirkung intermediärer Stoffwechselprodukte nach der Zufuhrung verschiedener Zuckerarten bei der Avitaminose). *Ibid.*, 278-290.

Extensive experiments reported in a dilute fashion lead the author to the belief that avitaminosis produces a disturbance of carbohydrate metabolism giving rise to intermediary toxic substances.—F. S. H.

(DIABETES) The demonstration of a hormone in plant tissue to be known as "glucokinin." Collip (J. B.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 321-323.

The author has extracted from plants a substance similar to insulin in its physiological action on the sugar metabolism of dogs and rabbits. This substance has been found in yeast, green onion tops, onion roots, barley roots, sprouted grain and several other plants. Collip concludes that it is probably present all through the plant kingdom. He suggests the name "glucokinin" for this substance. In some ways the author believes that it is superior to insulin when used to treat diabetic rabbits. It is less toxic and its effects are longer maintained.—J. C. D.

Case of **DIABETES** in pregnancy. Cortabarría (F.), Rev. méd. d. Uruguay (Montevideo), 1922, **25**, 611-616 (Aug.); abst., J. Am. M. Ass. (Chicago), 1922, **79**, 1645.

(**DIABETES**) Action of insulin on glycemia and on acidosis (Action de l'insuline sur la glycémie et sur l'acidose). Desgrez (A.), Bierry (H.) & Rathery (F.), Compt. rend. Acad. d. sc. (Par.), 1923, **176**, 1833-1835.

The usual results were obtained.—A. T. C.

Levulose in treatment of **DIABETES**. Desgrez et al., Bull. Acad. de méd. (Par.), 1922, **88**, 167-175 (October 31); abst., J. Am. M. Ass. (Chicago), 1922, **79**, 2196.

The variations of the blood sugar of the rabbit throughout the day and the effect of the subcutaneous injection of glucose. Eadie (G. S.), Am. J. Physiol. (Balt.), 1923, **63**, 513-519.—T. C. B.

(**DIABETES**) The influence of mono- and poly-saccharide on blood sugar (Über den Einfluss der Mono und Polysaccharide auf den Blutsucker). Eliassow (W.), Ztschr. f. klin. Med. (Berl.), 1922, **95**, 384-393; see also, München med. Wchnschr., 1922, **69**, 1508-1509.

Inulin usually has no influence on blood sugar. In a few cases a very slight increase was seen after 2-3 hours. When every day for 3 days about 25 gm. of inulin was given, the slight rise during the first and second days changed into a decrease on the third day. In 2 patients suffering from diabetes 100 gm. of inulin was given daily for 8 days; other carbohydrates were not given. The feces did not show a higher degree of fermentation after this diet. The author concludes that the action of inulin in the bowels is not yet completely understood, but that we have no reason to doubt that absorption takes place. It is very probable that absorption is very slow, and the author believes that this explains why inulin is supported so much better in diabetes than glucose or levulose.—J. K.

Relation of gallbladder disease to **DIABETES**. Eustis (A.), N. Orl. M. & S. J., 1923, **75**, 449; abst., J. Am. M. Ass. (Chicago), 1923, **80**, 957.

Syphilis of the **PANCREAS** (La syphilis du pancréas). Faroy (G.), J. méd. franç. (Par.), 1922, **11**, No. 12 (Dec.); abst., Presse méd. (Par.), 1923, **31**, 187.

(**DIABETES**) Hyperglycemia—Based upon a study of 2000 blood chemical analyses. Feinblatt (H. M.), J. Lab. & Clin. M. (St. Louis), 1923, **8**, 500-505.

The great majority of sugar determinations in this study were made by Folin's method. Out of 2000 routine blood sugar determinations taken in the wards of the Long Island College Hospital,

81 yielded readings in excess of 150 mg. per 100 cc. Thirty-four of the subjects, or 42 %, presented clinical evidences of diabetes mellitus. The remaining 47 were considered nondiabetic. These latter furnished a heterogeneous group, and in only 14, or 30%, could the diagnosis account for the hyperglycemia. A single report of an abnormally high blood sugar value may be due, among other things, to emotional disturbances. A study of the relation between hyperglycemia and glycosuria emphasizes the fact that the renal blood sugar threshold varies in different persons and in the same person under different circumstances. In diabetes a high threshold value may exist, which tends to increase in proportion to the severity of the disease.—I. B.

On the change in the nature of blood sugar of **DIABETICS** caused by **INSULIN**. Forrest (W. D.), Smith (W.) & Winter (L. B.), *J. Physiol. (Lond.)*, 1923, 57, 224-233.

The blood sugar of diabetics differs from that of normal persons as regards the ratio copper reducing to polarimetric value. In diabetics the decreased amount of blood sugar contains a greater proportion of normal blood sugar.—T. C. B.

White mice and the assay of **INSULIN**. Fraser (D. F.), *J. Lab. & Clin. M. (St. Louis)*, 1923, 8, 425-428.

The author finds that white mice starved 24 hours are very susceptible to the intraperitoneal injection of insulin and that mice fed immediately after the injection of insulin are very tolerant to its effects. Following the injection of insulin the starved mice, after a latent period of about 20 minutes, show postural eccentricities, increased rate and excursion of respiration, and finally either ataxia and paresis or convulsions. In a "typical" reaction the animal recovers within 5 minutes after the intraperitoneal injection of 0.25 cc. of 15% dextrose in 0.9% saline.—I. B.

(**DIABETES**) The presence of a blood sugar reducing substance in yeast. Funk (C.) & Corbitt (H. B.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1923, 20, 422-423.

The authors noted hyperglycemia in pigeons placed on a vitamin-free diet. The blood sugar was reduced by injections of vitamin B prepared from yeast. Since such yeast preparations act more slowly than insulin and over a longer period, as noted by Collip and others, it is suggested that the active substance is not identical with insulin but is a precursor which undergoes a slow change into it.—J. C. D.

DIABETES and tuberculosis. The problem of treatment. Funk (E. H.), *Med. Clin. N. Am. (Phila.)*, 1923, 6, 893-898.

In practically all cases of diabetes mellitus associated with pulmonary tuberculosis diabetes is the initial disorder and active tuberculosis a subsequent development. The problem of diet is vital.

Experience justifies the attitude of ignoring for the time being the tuberculosis in an attempt to render the urine sugar free by approved dietary methods. The resulting loss of weight need not disconcert the medical attendant, for it would inevitably occur if the diabetes were not controlled. Following dietary restrictions there is an increased ability to utilize carbohydrates and properly metabolize fat and proteins, and thus there may result not only a gain in weight, but an increased resistance to further extension and activity of the tuberculosis.—I. B.

Action of extracts of sclerosed PANCREAS on DIABETIC dogs (by extirpation of the pancreas) [*Action des extraits de pancréas sclérosé sur des chiens diabétiques (par extirpation du pancréas)*]. Gley (E.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1322-1325.

Reprint of a paper on this subject published by himself in February, 1905, and remarks on the work of Banting, Best, Macleod and others.—T. C. B.

The management of DIABETES MELLITUS of children. Graham (H. B.), *Med. J. Australia (Sydney)*, 1922, **ii**, 89-94; *abst.*, *Med. Sc. (Lond.)*, 1923, **7**, 361.

As regard the prognosis, although some investigators maintain that the diagnosis of diabetes in a child is practically equivalent to a sentence of death, Graham is less pessimistic.—R. G. H.

DIABETES and the THYROID (*Diabetes tiroidea*). Grau San Martín (R.), *Crón. méd.-quir de la Habana*, 1922, **48**, 493-495.

Treatment of DIABETES with diet and mineral waters (*Erfahrungen über die Diabetestherapie durch Diät und Mineralwasserkur*). Gaul (G.), *Allg. med. Centr.-Ztg. (Berl.)*, 1922, **91**, 127-129.

See *Endocrin.*, **6**, 678.

Transitory hypermetropia in DIABETES and its etiology (*Transitorisk hypermetropi ved diabetes og dens ætiologi*). Hagen (S.), *Norsk Mag. f. Lægevidensk. (Kristiania)*, 1921, **82**, 424-428.

Hagen suggests that transitory hypermetropia is more common in diabetes than is generally supposed, and within 6 months he has seen this combination in 3 cases in his private practice. In every case the hypermetropia did not develop till a starvation diet had been prescribed for about a week, and the concentration of sugar in the urine had been greatly reduced. This hypermetropia persisted for a month and a half to two months, being demonstrable long after the glycosuria had ceased. After giving details of these 3 and 2 other hospital cases, Hagen concludes that this form of hypermetropia must be the result of antidiabetic treatment, and not a direct sequel to the disease itself.—*Med. Sc.*, **7**, 359.

The rôle of phosphate and potassium in carbohydrate metabolism following INSULIN administration. Harrop (G. A. Jr.) & Benedict (E. M.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1923, **20**, 430-431.

(DIABETES) Hyperglycemia and hypertension. Herrick (W. W.), Tr. Ass. Am. Physicians (Phila.), 1923, May 1-2.

In the average case of diabetes mellitus, the blood pressure is low; but in the elderly obese patient with arterio-sclerosis, the blood pressure is high. From 10 to 25% of these people show a definite hyperglycemia, and constitute the borderline between hypertension and diabetes. They have a high sugar threshold. These are different from the essential hypertension cases. I have been impressed with the fact that these cases of obesity with hyperglycemia have often arisen from an ill balanced diet. These patients have been told that they must have diminished protein, and consequently they ingest more starchy foods. The effect on elderly persons with poor tolerance for glucose is dangerous. A condition of arteriosclerosis arises, with overstrain of the pancreas. These people are usually ambulatory office patients with circulatory embarrassment on account of obesity. If they are put on the diet that maintains the blood sugar at a normal level, loss of weight will result and there will be lowered blood pressure and less cardiovascular strain. An interesting point in blood chemistry is that the concentration of crystalloids in the blood is related to blood pressure. In plotting the curves of glucose and chlorid content of the blood, there is a definite relation between the two. There is a precise inverse concentration of chlorids and of sugar. Protein has heretofore borne all the odium in hypertension cases, but the possibility of overfeeding with carbohydrate in a certain class of cases has not been mentioned.

—J. Am. M. Ass., 80, 1804.

DIABETES MELLITUS und Urobilinogenuric. Hetényi (G.), Berl. klin. Wchnschr., 1921, 58, 1462-1463.

Hetényi, of the Third Medical Clinic of Buda Pesth University, examined 87 uncomplicated cases of diabetes and 14 with various complications, such as degeneration of the myocardium, uncompensated cardiac disease, alcoholism, and hyperemesis gravidarum, without finding a single case of urobilinogenuria. He comes to the conclusion that the liver in diabetes mellitus is in a condition of increased activity, inasmuch as it prevents the increased amount of urobilinogen, which under normal circumstances it could not deal with, from entering the blood-stream.—Med. Sc., 7, 359.

The mortality from DIABETES. Hoffman (F. L.), Boston M. & S. J., 1922, 187, 135-137.

Hoffman, consulting statistician to the Prudential Insurance Company of America, has drawn up a table of diabetes death rates for specified countries, in most cases for the five years ending 1919, showing that the range in frequency varies from a maximum of 38.4 per 100,000 of population in the case of the Island of Malta, 18.1 for the Isle of Man, and 16.1 for the Island of Guernsey, to a minimum of 1.5 for the Island of Jamaica, 1.1 for the Bahamas, and 1.0

for Venezuela. The average diabetes death rate for the United States registration area is 16.4 per 100,000 of population, practically the maximum rate attained by the countries or islands which rank highest in the table. The American death rate is decidedly above the average of 11.8 for England and Wales and while it is unquestionably affected by the relatively large Jewish population in the large cities of the United States, this factor cannot be considered as primarily responsible for the marked excess. As regards the mortality from diabetes in cities, the normal diabetic death rate of New York city for the five years ending 1919 was 19.8 per 100,000 population, or higher than the maximum rate reported for the city of Berlin (17.9), Copenhagen (17.1), or Amsterdam (15.9). The minimum rates were reported for Tokio (4.1), Singapore (4.3), Manila (4.5), and for the city of Mexico (5.4).—Med. Sc., 7, 355.

Glycosuria and DIABETES in exophthalmic goitre. Holst (J.), Acta med. Scand. (Stockholm), 1921, 55, 302-322.

The author observed at autopsy 4 cases of exophthalmic goitre combined with glycosuria. In all these cases there was found a decrease in the number of the Langerhans' islands and other histological changes of the pancreas. There is reason to believe that in Graves' disease the well-known anomalies in the sugar metabolism are induced by gross anatomical changes of the pancreas in some cases, whereas the slight anomalies are only functional. Seven patients suffering from Graves' disease with alimentary glycosuria were all cured by hemistrulectomy; 3 patients suffering from glycosuria became aglycosuric after the operation; another patient got diabetes, which proved fatal although she had previously undergone an operation for exophthalmic goitre. Thus the treatment shows good results in mild cases of glycosuria and poor results in severe cases. The glycosuria in experimental pancreas diabetes disappears or decreases after thyroidectomy. Normally the thyroid exerts an inhibitory action over the pancreas. These facts seem to favor the hypothesis that in the usual cases of non-thyrogenous diabetes also there is a therapeutic possibility in hemistrulectomy, not of curing the diabetes, but of reducing the hypofunction of the Langerhans' islands.—H. B.

The sugar content of cutaneous and venous blood in DIABETES MELLITUS and other forms of glycosuria (Undersøgelser over Sukkerindholdet i Cutanblod og Veneblod ved Diabetes mellitus og andre Glykosurier). Holst (J. E.), Hosp.-Tid. (Copenhagen), 1922, 65, 577.

In 1921, Hagedorn compared the sugar content of the capillary blood taken from a vein in the arm, and he found that the differences were not the same for diabetics and normal persons. In normal fasting persons the sugar content of the blood, taken simul-

taneously from these two sources, was practically identical. After the administration of carbohydrates and an increase of the sugar content of the blood, this was less in venous than in capillary blood, the difference in the two concentrations usually being greatest when the concentration of the sugar was highest. In normal persons (64 investigations) the difference ranged from 0.001 to 0.049, with an average difference of 0.026. He could find no regularity in these differences, great variations occurring not only in different persons but in the same person at different times. In diabetics the difference between the sugar content of the capillary and venous blood after the administration of carbohydrates was usually much smaller and was sometimes not demonstrable. The average difference for 26 investigations was 0.010. Hagedorn concluded that the composition of the capillary blood from the ear closely resembles that of arterial blood. Holst has carried his investigations a step further, his material consisting of 14 cases of diabetes mellitus and 23 of other forms of glycosuria. He confirms Hagedorn's finding that in diabetics given carbohydrates there is usually little or no difference between the sugar content of cutaneous blood and that of venous blood. The behavior in this respect of the 23 patients with non-diabetic glycosuria was essentially that of normal persons.—*Med. Sc.*, 7, 332-333.

The frequency of **DIABETES MELLITUS** in Basel (*Ueber die Häufigkeit des Diabetes mellitus in Basel*). Hunziker (H.), *Schweiz. med. Wchnschr.* (Basel), 1921, 52, 168-172.

As the result of a questionnaire addressed to all the medical practitioners and hospitals in the canton of Basle, Hunziker, of the Basle Public Health Office, gained the following information: (1) At least 1 per 1,000 of the inhabitants of the canton of Basle were suffering from diabetes mellitus in the period between April 1, 1918, and April 1, 1919; (2) the disease was considerably more frequent in the later decennia than in early life, 152 of the 215 patients being over 50 years of age; (3) in Basle, as elsewhere, diabetes mellitus is more frequent in males than females; (4) the Jewish population of Basle shows a very high diabetes incidence; the proportion of cases among Jews and non-Jews being 15:1 among men, 7:1 among women, and 12:1 in both sexes.—*Med. Sc.*, 7, 355.

Treatment of **DIABETES** in children. Johannsen (N.), *Acta Pædiat.* (Upsala), 1922, 2, 180.

Johannsen reports favorably on Joslin's method in the treatment of 7 diabetic children.—*J. Am. M. Ass.*, 80, 592.

Early diagnosis of **DIABETES**. John (H. J.), *Texas State J. M.* (Fort Worth), 1923, 13, 512-516; cit., *J. Am. M. Ass.* (Chicago), 1923, 80, 1271.

(DIABETES) Renal glycosuria. Jonas (L.), Med. Clin. N. Am. (Phila.), 1923, 6, 1079-1087.

An interesting paper of value in the differential diagnosis of diabetes mellitus. The importance of discrimination between renal glycosuria which does not influence the health of the individual, and diabetes mellitus is stressed. Blood-sugar tests are the indices in diagnosis.—I. B.

DIABETES MELLITUS complicating surgery. Jones (A. T.), Boston M. & S. J., 1923, 188, 483-488.

A discussion of the newer methods of treatment of DIABETES. Joslin (E. P.), South. M. J. (Birmingham), 1922, 15, 93-103.

The treatment of DIABETES. Joslin (E. P.), Boston M. & S. J., 1922, 186, 761-763; abst., Med. Sc. (Lond.), 1923, 7, 356.

Joslin states that in one series of his patients a third acknowledged that they had eaten or drunk to excess, and in another series two-thirds admitted excess in food.—R. G. H.

The urinary nitrogen excreted in DIABETES. Joslin (E. P.), Tr. Ass. Am. Physicians (Phila.), 1922, 37, 333-336.

From the study of a large series of urinary nitrogen determinations in diabetic patients the author concludes: (1) the protein metabolism alone does not control the total metabolism; (2) exogenous protein may be more stimulating to the metabolism than endogenous protein; (3) a very high nitrogen excretion in a severe and extremely thin diabetic may represent the prelethal rise of nitrogen; (4) even a feeble and famished diabetic may still retain the power to oxidize carbohydrate to a degree which is often not appreciated, but should be utilized. It is not how much fat a diabetic can bear, but how much carbohydrate he can burn which should engage our attention. If he can burn carbohydrate in a prelethal state he should certainly burn it when in better nutrition. In diabetes our chief concern is the oxidation of carbohydrate.—I. B.

Levulose and the DIABETIC metabolism. Joslin (E. P.) & Root (H. F.), Tr. Am. Soc. Clin. Investigation, 1923, April 30.

Highly purified levulose in amounts proportional to body weight was given to diabetic patients. Levulose ingestion produced a less marked hyperglycemia than dextrose, and a marked rise in respiratory quotient and metabolism followed. Even in severe diabetes, only a small amount of sugar appeared in the urine after as much as from 75 to 100 gm. of levulose was taken. Pure levulose, 15 gm. in portions of 5 gm., 3 times daily, or insulin, 15 gm., in the form of artichokes when added to the diet of a diabetic patient for periods of from one to four weeks did not produce glycosuria.

—J. Am. M. Ass., 80, 1727.

Influence of infection on carbohydrate tolerance in DIABETES MELLITUS. Kern (R. A.), *Med. Clin. N. Am.* (Phila.), 1923, 6, 1053-1066.

A report of 2 cases. In case 1, that of a man of 65, diabetic gangrene developed following the blistering of the toes by a hot brick. After a course of preliminary dieting, amputation was performed following which, despite the absence of any particular dietary attempt to render the urine sugar free, there was increased carbohydrate tolerance and disappearance of glycosuria and ketonuria. Case 2 is that of a girl of 13 who, while on an inevitable high-fat diet, developed an infection of the throat which terminated fatally in 6 days in diabetic coma. The author points out that the patient required the high-fat diet prior to the occurrence of the complication, but that it rendered her more vulnerable to infection.

—I. B.

A case of infantile DIABETES (Ein Fall von Diabetes im Säugling-salter). Kochmann (R.), *Jahrb. f. Kinderh.* (Berl.), 1922, 99, 20-27; abst., *Med. Sc.* (Lond.), 1923, 7, 360.

Kochmann, who reports a fatal case in an infant aged 4½ months, in whom death was preceded by staphylococcal folliculitis, bronchopneumonia, and coma, states that the disease is extraordinarily rare during the first year of life, only 6 cases of the kind, and none of them above criticism, having been collected by Stern. The diagnosis in Kochmann's case was based on the persistent excretion of glucose, and was confirmed by the autopsy, which showed a great deficiency of the islands of Langerhans and the presence of fatty changes in the liver and kidneys. The author maintains that the life of a diabetic child can be prolonged only for a few months even by the best treatment.—R. G. H.

DIABETES MELLITUS and icterus. Koleczek (A.), *Monatschr. f. Kinderh.* (Leipz.), 1923, 26, 68-70.

A case described in a boy of six.—J. K.

Insulin in treatment of DIABETES. Krogh (A.), *Ugesk. f. Laeger* (Copenhagen), 1923, 85, 21-25.

Krogh relates the history of this new treatment of diabetes, of which he made a special study while in this country. Probably it will be long before insulin can be imported into Denmark. He discussed with the Toronto professors the possibility of Danish collaboration in further research, especially in the use of fish instead of beef pancreas. In collaboration with Drs. Hagedorn and Johansen the work is now well under way at Copenhagen, with both fish and beef pancreas.—J. Am. M. Ass., 80, 592.

Renal DIABETES during pregnancy in its relation to the functions of the ENDOCRINE GLANDS (Der renale Diabetes während der

Schwangerschaft in seiner Abhängigkeit von den Funktionen der Drüsen mit innerer Sekretion). Küstner (H.), Monatschr. f. Geburtsh. u. Gynäk. (Berl.), 1923, 62, 119-126.

Pregnant rabbits show renal glucosuria. The increased sensitivity of the kidneys is not caused by the placenta or fetal metabolic products, but by an altered function of the ovary. Renal diabetes is dependent upon the presence of a corpus luteum.—F. S. H.

Acidosis from fasting and from DIABETES. Labbé, Bull. Acad. de méd. (Par.), 1923, 89, 242-255; abst., J. Am. M. Ass. (Chicago), 1923, 80, 1882.

Variations in glycemia under the influence of fats in DIABETES (Variations de la glycémie sans l'influence des graisses chez les diabétiques). Labbé (H.) & Théodoresco (B.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 483-484.

DIABETES in children and its treatment (Le diabète infantile et son traitement). Labbé (M.), Paris méd., 1922, i, 371-378; abst., Med. Sc. (Lond.), 1923, 7, 360.

Labbé remarks that while diabetes in children does not differ fundamentally from that met with in adults it is practically only the severe form which is seen in children, whereas in the adult the bulk of the cases are moderate or mild and show no tendency to progress. Although the disease is not frequent in children, Labbé has seen about 30 cases. Exceptionally it may occur during the first weeks of life, and its frequency increases with age. According to Labbé, congenital syphilis is not of any greater importance in the pathogenesis of infantile diabetes than acquired syphilis in the etiology of adult diabetes. Heredity appears to have more significance, although it is not frequent to find a diabetic patient producing a diabetic child. In 3 of his patients the disease occurred in several members of the same family. Labbé emphasizes the insidious character of the onset of diabetes in children. The child loses flesh and appears to be tired, the digestion is often defective and the general development is inadequate, often amounting to infantilism. Some maintain that the diagnosis of diabetes in a child is practically equivalent to a sentence of death, but Labbé is less pessimistic.—R. G. H.

The action of levulose in DIABETES (L'action du lévulose chez les diabétiques). Labbé (M.), Bull. Acad. de méd. (Par.), 1922, 88, 189-193; abst., Presse méd. (Par.), 1922, 30, 978.

Although levulose is better tolerated by diabetics than are certain other sugars, it is not completely utilized and its absorption provokes a hyperglycemia and glycosuria which is not very different from that produced by glucose. Like all other hydrocarbons, levulose exercises an antiketogenic action on the acidosis of fasting; but

there is no influence on diabetic acidosis, the pathogenesis, intensity and seriousness of which are quite different. The equilibrium of the diet is of great importance from the point of view of the acidosis of fasting, but is not of the same significance as in diabetic acidosis, the mechanism of which is very difficult to study.—R. G. H.

DIABETES and syphilis. Labbé (M.), Bull. Acad. de méd. (Par.), 1923, 89, 53-60; abst., J. Am. M. Ass. (Chicago), 1923, 80, 878.

DIABETIC hyperglycemia (*La glycémie chez les diabétiques*). Labbé (M.), Labbé (H.), Nepveu (F.), Presse méd. (Par.), 1923, 31, 173-174.

The value of the clinical information furnished by glucose tolerance tests is discussed; it is shown that these tests alone reveal the efficiency of sugar metabolism, but it should be recalled that anomalies of sugar metabolism are not found exclusively in diabetes, since such anomalies have been observed in liver insufficiency by Gilbert and Baudoin, and in Graves' disease by American investigators. The writers point out that the relation between glycemia and glycosuria is too variable to give information of any value; they cite their observations on 3 diabetics with equal blood sugar values, who were found to excrete respectively 2.51 gm., 18.9 gm. and 30.16 gm. of sugar in each 1000 cc. of urine; another patient was found to excrete 4.41 gm. at one time and only 2.11 gm. at another time, although his blood sugar remained constant at 1.55-1.56 gm. The relative permeability of the kidney to glucose (renal threshold) only partly explains these variations; Ambard's conception of the extreme variability of the renal threshold seems somewhat exaggerated, because, as in many biologic phenomena, the initial threshold, marked by the appearance of sugar in the urine, is always higher than the final threshold, marked by the disappearance of sugar. Some writers believe that the duration of the diabetes raises the renal threshold, but it seems more probable that the increased impermeability of the kidney is the result of the nephritic complications, which are far more common in mild, slow types of diabetes than in rapid, severe types. Study of the renal threshold has furnished the following classification: (1) ordinary diabetes, which may be mild or severe, with or without derangement of protein metabolism, but in which the threshold remains at 2 gm. per 1000; (2) the diabetes of obesity complicated by nephritis, in which the renal threshold is permanently high, as shown by excessive hyperglycemia with or without very mild glycosuria, and which points to a severe derangement of sugar metabolism; and (3) renal glycosuria, caused by hyperpermeability of the kidney in the absence of disturbances of sugar metabolism. Glycose tolerance tests are of value also by revealing the patient's response to treatment.—G. L.

The rôle of syphilis in the etiology of **DIABETES** (*Le rôle de la syphilis dans l' étiologie du diabète*). Labbé (M.) & Toufflet (H.), *Ann. de méd.* (Paris), 1923, **13**, 567-582.

An exhaustive critical study. It is concluded that in the great majority of cases syphilis plays no part in the genesis of diabetes: statistics show that syphilis is no more frequent among diabetics than other diseased persons and that diabetes does not occur with any particular frequency among the syphilitics. Clinical practice shows the inefficacy of specific treatment for diabetes. The similitude of the nervous symptoms in the two diseases is no argument for attributing diabetes to syphilis. Conjugal diabetes is sufficiently explained on the basis of a common hygienic defect. There are, however, certain cases of syphilitic diabetes. They are the sequence of syphilitic lesions of the pancreas, liver and nervous system. These cases are very rare, and are particularly interesting from the fact that specific treatment is curative.—F. S. H.

(**DIABETES**) Fat carbohydrate ratio. Ladd (W. S.) & Palmer (W. W.), *Tr. Ass. Am. Physicians* (Phila.), 1921, **36**, 266-268.

DIABETES and syphilis (*Diabète et syphilis*). Lebar. *Vie méd.* (Par.), 1921, **2**, 1063-1065.

Dietetic treatment of **DIABETES**. Linossier (G.), *Paris méd.*, 1922, **12**, 265-271 (September 23); abstr., *J. Am. M. Ass.* (Chicago), 1922, **79**, 2039.

Insulin and **DIABETES** (*Insulin und Diabetes*). Lux (A.), *Wien. klin. Wchnschr.*, 1923, **36**, 297-298.

Describes American investigations.—J. K.

The respiratory exchange and blood sugar curves of normal and **DIABETIC** subjects after epinephrin and insulin. Lyman (R. S.), Nicholls (Elizabeth) & McCann (W. S.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, **20**, 485-488.

The article gives the details of tests carried out on 5 normal men and 8 diabetics.—J. C. D.

The treatment of **DIABETES MELLITUS**. Lyon (D. M.) & Meakins (J.), *Edinb. M. J.*, 1921, n. s., **27**, 270-285.

The authors describe the Allen treatment, noting recent modifications and illustrating the method with a case history.—J. C. D.

PANCREATIC extract and **DIABETES**. Macleod (J. J. R.), *Canad. M. Ass. J.* (Toronto), 1922, **12**, 423-425.

After mentioning the experimental preparation of extract and the difficulties encountered in passing to large-scale production, the author continues: "But the most significant of the results which have been obtained are as follows: Subcutaneous injection of the extract into normal rabbit causes a certain level (about 0.045 per

cent), perfectly characteristic symptoms of a convulsive character appear and, if left alone, the animal passes into a comatose condition, which soon ends in death. If a solution of sugar be injected subcutaneously when the symptoms appear, the animal immediately recovers and may remain perfectly normal or pass again into the convulsions, which may be removed a second time by injections of sugar. Many observations have convinced us that these symptoms are definitely related to the lowering of blood-sugar—they may indeed be called hypoglycaemic convulsions—and this is all the more interesting in the light of the work of F. C. Mann, who found similar symptoms to develop in dogs when the blood sugar was lowered to about 0.04 per cent by isolation of the liver from the circulation. The discovery of this effect on normal rabbits has proved a most important one in connection with the isolation and purification of the extract, since it affords a readily available laboratory test object. It obviates the necessity of using depancreated dogs for our work. As is to be expected, an extract which acts only feebly on normal rabbits has a much more pronounced effect on the hyperglycaemia of diabetic dogs. Not only is the blood sugar lowered in rabbits that are normal but also in those rendered diabetic by any of the experimental methods usually employed to bring this about. These are puncture of the floor of the fourth ventricle (piqûre), asphyxia, poisoning by carbon monoxide gas, ether, or adrenalin. None of these causes hyperglycaemia in rabbits after injecting them with sufficient amounts of pancreatic extract. There may occasionally be a slight increase in the percentage of blood sugar but never to anything like the extent usually observed without extract. The animals used for these experiments were always well fed with carbohydrates and the glycogen content of the liver determined. The importance of this result is that it shows us that even the purely experimental forms of diabetes have much in common with the clinical forms."

The results of glycogen and fat analyses are discussed as follows: "The importance of these observations rests on the fact that they show that the function which is primarily regulated or controlled by the internal secretion of the pancreas is that concerned with the deposition of glycogen. They would seem to suggest that glycogen must be an essential preliminary stage in the utilization of sugar by the animal body and that when the pancreatic hormone is absent excess of sugar leads to the mobilization of large quantities of fat."

After mentioning the observations of elevation of the respiratory quotient the author concludes: "In the light of these various types of evidence we feel justified in expressing the belief that it will be possible by administration of pancreatic extract, to treat diabetes in man much more satisfactorily than has hitherto been the case. Dietetic control must no doubt remain an important feature of treat-

ment, and will probably be all that is necessary in the earlier stages of the disease, but in the later stages it is hoped that administration of extract will prove of value. What other therapeutic uses the pancreatic extract may have remains as yet undetermined."—J. Metab. Research, 2, 137-138.

(DIABETES) Response to two notes of R. Carrasco-Formiguera entitled "Critique de quelques points de la doctrine de Maignon sur l'acétonurie." "Etude de l'équilibre acétogénique et anti-acétogénique dans le métabolisme de l'animal diabétique spontané." Maignon (F.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 877-880.—T. C. B.

(DIABETES) Studies on sugar tolerance. Major (R. H.), Johns Hopkins Hosp. Bull. (Balt.), 1923, 34, 21-26.

The results of glucose tolerance tests on 60 patients are reported. The diabetic type of sugar curve with glycosuria is constant in diabetes mellitus. The level of the sugar threshold varied greatly, showing a tendency to be higher in older individuals. All the cases of acute nephritis studied showed a diabetic type of blood sugar curve usually without glycosuria. No constant type of curve was obtained in thyroid or pituitary diseases. Abnormal curves are frequent and indicate a disturbance of carbohydrate metabolism. Increased tolerance to carbohydrates was found in pituitary disease, often with a high sugar threshold. Some of the glycosurias encountered in hyperthyroidism are due to a lowered renal threshold. These observations indicate that as a rule the urine does not show sugar in appreciable amounts until a definite blood sugar level is reached. This level or "renal threshold" varies somewhat in health, but markedly in disease. Repeated tests on the same individuals show marked variations in this "renal threshold." Four individuals classed as "renal diabetics" showed glycosuria with a blood sugar at normal or subnormal levels.—Author's Summary.

CHRONIC PANCREATITIS. Marsh (P. L.), Med. Clin. N. Am. (Phila.), 1923, 6, 1223-1225.

An interesting contribution of special value to the surgeon, dealing with the casual relationship between diabetes mellitus on the one hand and gall bladder disease and chronic pancreatitis on the other. Three illustrative case histories are included.—I. B.

The relation between ingested fat and the lipemia of DIABETES MELLITUS. Marsh (P. L.) & Waller (H. G.), Arch. Int. Med. (Chicago), 1923, 31, 63-75.

Twelve patients of varying age, with different types of diabetes mellitus as regards severity, previous treatment, degree of acidosis and duration of symptoms, form the basis for this study. All were for some time on the Newburgh and Marsh high fat, low protein,

low carbohydrate diet. The total lipoids of the blood were determined by the method of Bloor. Charts of each case are included, which graphically demonstrate that in the patients in whom hyperlipoidemia existed at first observation, the total blood fat had later diminished to normal levels despite the fact that the food fat was progressively increased. This is strong evidence that the prevalent assumption that diabetic hyperlipoidemia is dependent on the excessive ingestion of fat is unwarranted. The explanation of this phenomenon must be sought in some other unusual feature of the diabetic state.—H. L.

Treatment of mild DIABETES MELLITUS. Marsh (P. S.), J. Mich. M. Soc. (Grand Rapids), 1923, 22, 56-61; cit., J. Am. M. Ass. (Chicago), 1923, 80, 957.

Non-specific Wassermann reactions in DIABETES MELLITUS. Mason (E. H.), Am. J. M. Sc. (Phila.), 1921, 162, 322-328.

Mason states that in a series of 168 cases of diabetes mellitus treated at the Metabolism Clinic of the Royal Victoria Hospital, Montreal, 2 gave strongly positive Wassermann reactions in the blood, though there was no history or evidence of syphilis. In both cases the reaction became negative after slight antisyphilitic treatment (2 intravenous injections of neophenarsenyl), but there was a marked and rapid decline of the carbohydrate tolerance. Mason suggests that the arsenic acted as a toxic agent upon the weakened pancreatic cells, altering the quality or quantity of the internal secretion.—Med. Sc., 7, 360.

(DIABETES MELLITUS) Respiratory exchange following the ingestion of glucose, glycerol, calcium hexose phosphate and calcium glycerophosphate. McCann (W. S.) & Hannon (R. R.), Johns Hopkins Hosp. Bull. (Balt.), 1923, 34, 73-80.

In a study of the effects of glucose ingestion on the respiratory exchange of diabetic subjects two types of response were encountered. In the first type of subject, ingestion of glucose resulted in a diminished rate of carbohydrate oxidation, as shown by a decrease in the respiratory quotients for an abnormal length of time. These subjects all improved greatly under treatment with the development of a good carbohydrate tolerance, showing on subsequent tests an improved ability to oxidize glucose. A second type of patient with severe diabetes was encountered in whom the ingestion of glucose produced a rise of respiratory quotients at a rate similar to that of normal subjects. These individuals were not responsive to treatment with a maintenance diet, low in protein, and balanced as regards ketogenic and antiketogenic factors. A rise in heat production may or may not follow the ingestion of glucose by diabetic subjects. It occurred in both subjects of the second type. In the first type the heat production may increase with falling respiratory quotients and

vice versa. The changes in respiratory quotients of diabetic subjects who ingested glycerol were parallel to those produced by the ingestion of glucose in the same subjects. In normal subjects there was no parallelism between the effects of glycerol and glucose. The specific dynamic action of glycerol was negligible in all but one experiment. In this one case an increase in total metabolism of 20% was observed coincidentally with a decrease in R. Q. A comparison of the effects of ingestion of calcium hexose phosphate with those produced by glucose showed that in subjects of the first type hexose from the phosphoric ester was oxidized more readily than glucose. Hexose phosphate ingestion caused a steady rise in respiratory quotients in both diabetic subjects and in a normal individual. It was followed by a rise in heat production of from 4.5-12% in all experiments. The effect of the ingestion of calcium glycerophosphate upon the respiratory exchange is variable. In three diabetic subjects of the first type the respiratory quotients rose more readily than when glycerol was taken alone. It is impossible to interpret these results in terms of the oxidation of glycerol.—Quoted from original.

The use of a high fat diet in DIABETES MELLITUS, with report of a case. McCollom (W. E.), Long Island M. J. (Brooklyn), 1922, 16, 99-103.

A review of the current methods.—J. C. D.

The influence of the nutritional condition of the animal on the hypoglycemia produced by INSULIN. McCormick (N. A.), Macleod (J. J. R.), Noble (E. C.) & O'Brien (K.), J. Physiol. (Lond.), 1923, 57, 234-252.

Toxic symptoms are more frequent or occur earlier in rabbits having a scanty store of glycogen than in those having an abundance of glycogen. With small doses of insulin the blood sugar may be scarcely affected in glycogen rich animals, but show a pronounced fall in non-glycogenic animals. For a period varying from 30 to 90 minutes after injection of insulin the sugar falls at a uniform rate and bears no relation to dose or nutritional condition of the animal. After this it rises more rapidly in glycogen rich animals. An approximate assay can best be arrived at by measuring the blood sugar 90 minutes and 3 hours after injection in animals that have fasted 24 hours.—T. C. B.

The present status of insulin therapy in DIABETES. McLean (F. C.), China M. J. (Shanghai), 1923, 37, 205-214.

An excellent review. An announcement of the forthcoming preparation of insulin by the Peking Union Medical College is made.

—L. G. K.

Syphilitic DIABETES MELLITUS. Meineri (P. A.), Policlin. (Roma), 1923, 30, 307.

Meineri relates an unusual case of diabetes mellitus of syphilitic origin in a man, aged 46, the fifth year after infection with syphilis. He had taken courses of calomel during these years, but then symptoms of diabetes developed, with symptoms of neurosyphilis. Under intensive arsenical-mercurial-iodid treatment the whole subsided. Treatment as for diabetes had no effect, but under the specific treatment the glucose in urine dropped from 88 to 44 gm. and finally disappeared entirely during the last week of the course. He cites Villaret's recent case in which symptoms of diabetes appeared a few days after the primary chancre. The glycosuria of 422 gm. and the acetonuria rapidly subsided under mercurial treatment. In his case he ascribes the diabetes to syphilitic lesions in the central nervous system. The cerebral symptoms disappeared first, then the glycosuria, but the Wassermann reaction was still strongly positive 2 months later.—J. Am. M. Ass., 80, 1816.

Glucose tolerance test in DIABETES. Menninger (C. F.), Kansas M. Soc. J. (Topeka), 1923, 23, 85-90; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1732.

Type of diet as an etiologic factor in DIABETES MELLITUS. Meyer (J. E.), Nebraska State M. J. (Norfolk), 1923, 8, 89-93; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1342.

• **Decreased intraocular tension in DIABETIC coma.** Middleton (W. S.), Wisconsin M. J. (Milwaukee), 1923, 21, 458-459; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1414.

Psychologic tests applied to DIABETIC patients. Miles (W. R.) & Root (H. F.), Arch. Int. Med. (Chicago), 1922, 30, 767-777.

Diabetic patients frequently complain of poorer memory and diminished power of attention, but objective proof of this has been lacking. By certain psychologic tests applied in such cases as well as to suitable controls, it was found that diabetic patients with hyperglycemia and glycosuria at the beginning of treatment show a decrement of about 15% or more in memory and attention tasks. The loss is in amount rather than in quality. With treatment the diabetic improves rapidly in his psychologic status, approaching but not quite reaching normal. In accuracy and quickness of movements five treated diabetics, each case of long duration, were 20% below normal.—H. L.

Clinical indications of the etiology of DIABETES. Mitchell (J. W.), Med. Rec. (N. Y.), 1921, 100, 575-580; abst., Med. Sc. (Lond.), 1923, 7, 356.

The predilection of diabetes for the male sex is shown by the fact that of Mitchell's 116 cases, 70 were males and 46 females.

A definite history of diabetes in several members of the family was obtained in 46.6% of the cases. Sixty-five, or 56% of the patients were Jews. Approximately 60% were obese or gave a history of obesity. Fifty-one, or 43.9% gave a history of recent infection, such as influenza, gall-bladder infection, or gastro-intestinal disease; syphilis figured in only 3 of his cases.—R. G. H.

Treatment of DIABETES by the active extract of the Isles of Langerhans (*Quelques considérations à propos des récents travaux canadiens sur le traitement du diabète par l'extrait actif des îlots de Langerhans*). Monad (G.), Bull. gén. de thérap. (Par.), 1923, 174, 100-101.

Symptomatology and treatment of infantile DIABETES (*Séméiologie et traitement du diabète infantile*). Mouriquand (G.), Lyon méd., 1922, 131, 3-13.

The author remarks that polyuria is almost constant and is often the first symptom to attract attention. Polydipsia is another early sign which is rarely absent. Polyphagia, on the other hand, is less constant than polyuria or polydipsia, and is a late phenomenon. Pain in the epigastrium, in Mouriquand's experience, is commoner in the child than in the adult. On the other hand, boils, abscesses, and trophic lesions are less frequent in the child and usually appear only towards the end of the disease. The nervous system is also less frequently affected in the child, intense and obstinate headache being often the only symptom of this kind. As regards the prognosis, Mouriquand maintains that the diagnosis of diabetes in a child is practically equivalent to a sentence of death.—Med. Sc., 7, 360.

Treatment of DIABETES (*Behandling av diabetes*). Motzfeldt (K.), Norsk Mag. f. Lægevidensk. (Kristiania), 1921, 82, 249-284.

Motzfeldt, of the Rikshospital, Christiania, has carried out the modern starvation treatment of diabetes, as advocated by American writers, during the past 3½ years, and has compared the results achieved in this period with those of the earlier period 1912-1917, when such systematic dieting was not prescribed. In the first period there were 54 patients whose average age was 44. In the second period there were 77 patients whose average age was 36, and whose disease in many cases was severe. In the first series only 44% were discharged without glycosuria and ketonuria, in the second series 79%. In the first series 24%, in the second series only 9%, were discharged with glycosuria and ketonuria. In the first series 13%, and in the second series only 5%, died in coma. Motzfeldt supplements these statistical data in favor of modern starvation treatment and total dietary restrictions with illustrative cases of diabetes which a few years ago would have been regarded as inevitably and rapidly fatal. A valuable and simple clinical test in cases of acidosis threatened with coma is to note the time the patient can hold his breath

Although Motzfeldt's paper is largely confirmatory of Allen's system, he does not push dieting to such an extreme as Allen seems to find advisable.—Med. Sc., 7, 361.

Aqueous extracts of the PANCREAS. 1. Influence on the carbohydrate metabolism of **DEPANCREATIZED** animals. Murlin (J. R.), Clough (H. D.), Gibbs (C. B. F.) & Stokes (A. M.), J. Biol. Chem. (Balt.), 1923, 56, 253-296.

Acid aqueous extract of cat's pancreas raised the respiratory quotient in 2 different cats from the diabetic level to 0.82 and 0.87. Extracts of pig and ox pancreas were about equally effective for reducing the blood sugar and the D:N ratio of depancreatized dogs when given intravenously, subcutaneously or intraperitoneally. Extracts made in acidulated water were just as effective as those made in acidulated alcohol. Extremely toxic effects are obtained if the trypsin is not destroyed or if the acid is not completely neutralized before administration. Filtering through charcoal and Lloyd's reagent removes a large part of the active principle. There are 2 substances in the aqueous extracts, one of which lowers the blood sugar and the D:N ratio and raises the respiratory quotient; the other raises the blood sugar of both normal and depancreatized animals and possibly causes an abrupt fall in the respiratory quotient to the diabetic level after 3 to 5 hours. The method of stomach administration has given almost uniformly positive results.—F. S. H.

Influence of acid perfusates upon the blood sugar, D:N ratio and respiratory metabolism of **DEPANCREATIZED dogs.** Murlin (J. R.), Clough (H. D.), Gibbs (C. B. F.) & Stone (N.), Am. J. Physiol. (Balt.), 1923, 64, 348-363.

Insulin is extracted by perfusion of the pancreas with acidulated Ringer more readily than with alkaline. There is sufficient concentration of insulin to cause a fall of blood sugar.—T. C. B.

On the mechanism of phlorizin **DIABETES.** Nash (T. P.) & Benedict (S. R.), J. Biol. Chem. (Balt.), 1923, 55, 757-767.

Using dogs as experimental animals it was found that dextrose ingested in sufficient amount to induce protracted hyperglycemia in phlorizinized animals is recovered quantitatively in the urine. It is suggested that phlorizin not only affects the permeability of the kidney tissue of blood sugar, but produces an intrinsic impairment of the sugar-burning mechanism. When a mixture of dextrose and urea is ingested by a phlorizinized dog the sugar is excreted in the urine more rapidly than the urea. This discredits the interpretation of a more rapid production of sugar than urea in animo-acid metabolism.—F. S. H.

Metrorrhagias in **DIABETES (*Metrorrhagias en la diabetes*).** Navarro (A.), An. Fac. de med. (Montevideo), 1923, 8, 171-174.

Report of 3 cases.—R. G. H.

Dietary treatment of DIABETES. Nesbit (W. E.), Texas State J. M. (Fort Worth), 1923, 13, 516-518; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1271.

Recent advances in dietetic treatment of DIABETES MELLITUS. Neuhoﬀ (F.), J. Missouri M. Ass. (St. Louis), 1923, 20, 57-59; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1101.

Cases illustrating the use of a high fat diet in the treatment of DIABETES MELLITUS. Newburgh (L. H.), Med. Clin. N. Am. (Phila.), 1923, 6, 1119-1127.

While the method of fasting and undernutrition has its advantages in the treatment of especially the severer forms of diabetes, theoretic considerations suggest that moderate restriction of calories during the period of desugarization will accomplish as much as complete fasting, and that a maintenance diet will be just as capable of keeping the patient sugar free and of preventing or delaying downward progress as will undernutrition. Moreover, a dietetic regime that will control this disease while avoiding the evil of incapacity is desirable. A diet of this sort must be much higher in fat and poorer in protein than that administered in the past. Four case histories of the 200 consecutive patients treated by the high fat, low protein, low carbohydrate diet are given as evidence that this diet not only does not cause acidosis, but is attended by its disappearance in those patients who were suffering from acidosis at the start.—I. B.

Further observations of the use of a high fat diet in the treatment of DIABETES MELLITUS. Newburgh (L. H.) & Marsh (T. L.), Tr. Ass. Am. Physicians (Phila.), 1922, 37, 117-165.

Though overfeeding and large gains in weight are detrimental to the diabetic, severe undernutrition is likewise harmful. A suitable diet may be constructed by deriving the major portion of the calories from fat. Ample evidence is offered to prove that the fear of fat in the dietary of the diabetic is groundless. Recent findings confirm the authors' previous conclusions that a high fat dietary succeeds in controlling glycosuria, avoiding acidosis, maintaining nitrogen balance, and avoiding or overcoming hyperlipoidemia and permits normal activity on the part of the patient. Some patients who could not be made sugar free by starvation may be made so by a high fat diet yielding about 950 calories. The prognosis of diabetes is also discussed in detail, as well as many practical points relative to cooperation of the patient in treatment.—I. B.

DIABETES in children. Nobécourt, Bidot & Paraf, Arch. latino-am. de pediat. (Buenos Aires), 1922, 16, 705-710 (November).

The authors call attention to diabetes with arrest of growth, in children. A typical case is described in which the girl, aged 15, appeared to be but 12. The diabetes developed at the age of 13. The

child was fairly well nourished, but it was impossible to free the urine from sugar. Loss of weight and general depression followed too strict dietetic measures.—*J. Am. M. Ass.*, 80, 514.

Treatment of DIABETES by the general practitioner (*Hausärztliche Behandlung des Diabetes*). v. Noorden (C.), *Deutsche med. Wchnschr.* (Berl.), 1923, 49, 69.

von Noorden believes that hereditary diabetes is caused by hereditary pancreatic weakness. Children of diabetic families ought to live on a diet low in carbohydrates and rather low in protein as infections may reach the pancreas, causing temporary glycosuria and sometimes, many years later, producing real diabetes. The overfeeding so often practiced after infectious diseases is not recommended. The author denies the existence of neurogenic diabetes; he considers renal diabetes as a light case of real diabetes. The different methods of treatment are discussed. In coma the author advises lavage of the stomach, alcohol, but no food, even no carbohydrates, and, when necessary, strophanthin.—J. K.

The internal secretion of the PANCREAS (*Experimentelles Studium der inneren Sekretion des Pankreas. II. Über den Kohlenhydratstoffwechsel bei den Hunden mit der Ecksehen Fistel*). Oka (T.), *Tohoku J. Exper. Med.* (Sendai), 1922, 3, 206-225; abst., *Ber. ü. d. ges. Physiol.* (Berl.), 1923, 16, 471.

The PANCREATIC hormone and DIABETES (*Hormone pancreatique et diabète*). Pagniez (P.), *Presse méd.* (Par.), 1923, 31, 50-51.

A historical survey of the progress made in the study of diabetes, beginning with the experiments of Mering and Minkowski, 1889, and ending with the discovery of insulin by Banting and Best with reference to the studies of Collip and Macleod. The work of Hédon, 1891, who produced chronic diabetes in dogs by partial pancreatectomy, and of Lépine, who suggested that lack of a pancreatic hormone was the cause of diabetes, is discussed. Mention is also made of the recent experiments of Mackenzie Wallis, who used an alcoholic extract of hogs' pancreas with some success in diabetes and showed that it produced glycolysis in vitro, and of the work of Thomson, who used a boiled pancreatic extract which caused hypoglycemia in rabbits and severe headaches in his experiments on himself. The writer raises the question as to how far the effect of pancreatic extracts are to be considered specific, since he obtained similar results with peptons and salvarsan; he noted, however, that the clinical results produced in certain types of diabetes cannot be questioned.

—G. L.

DIABETES MELLITUS with slight acidosis. A discussion of the buffers of the blood. Pepper (O. H. P.), *Med. Clin. N. Am.* (Phila.), 1923, 6, 926-931.

A discussion of the known principles involved in the biochemistry of diabetes mellitus, with an illustrative case.—I. B.

Dietetic treatment of DIABETES (*Dietetische behandeling der suikerziekte*). Peters (J. T.), *Nederl. Tijdschr. v. Geneesk.* (Haarlem), 1922, 66 (II), 2569-2584.

No new data. A combination of different methods is recommended.—J. K.

The beginnings of arthritic DIABETES (*Les débuts d'un diabète arthritique*). Perrin (M.), *Rev. méd. de l'est* (Nancy), 1921, 49, 634-635.

Brief note concerning the record of urinary analyses in a case of diabetes from 1899 to 1917. The interesting point in connection with the observation is the marked effect of emotional excitation in increasing the glucosuria.—F. S. H.

The "N-minimum" in DIABETES MELLITUS. Petrén (K.), *Acta med. Scand.* (Stockholm), 1922, Suppl. III, 101-112.

The author examined the excretion of urea in 30 cases of diabetes. He concluded that it is possible to obtain a lower N-minimum in diabetes than under normal conditions. It is not necessary to give the patients an excessive quantity of calories; even when the food is greatly reduced, urea excretion is low. Nor is a great quantity of carbohydrates needed. Thus it is easier to induce a minimum nitrogen metabolism in the diabetic organism than in the normal one. The author noted decreased nitrogen metabolism in hunger even when the urea excretion was previously very low, whereas a small amount of albumen added to the food had the power of increasing the metabolism.—H. B.

Syphilitic origin of DIABETES (*L'origine syphilitique des diabètes*). Pinard (M.), *Médecine* (Par.), 1922, 4, 123-124.

Pinard believes that the incidence of syphilis as a cause of diabetes is sufficiently high that it should always be treated or ruled out before dietary treatment is instituted.—R. G. H.

Relations between the PANCREAS and neurosis, heart neurosis, Graves' disease and nervous diarrheas (*Über die Beziehungen des Pankreas zu Neurosen, Herzneurosen, Basedowoid, nervösen Diarrhöen*). Pineles (F.), *Wien. Arch. f. inn. Med.*, 1923, 6, 167-174.

The case is described of a man of 51 who, since 30 years of age, had shown several symptoms of heart neurosis. The urine was without albumin or sugar. There was no goiter. About 7 years ago temporary glycosuria was noted. Six years ago the ingestion of

100 gm. glucose produced glycosuria; 3 years ago this reaction was negative. Since 1 year ago the patient has had diabetes. A man of 56 was observed. When he was 24 he had his first attack of stenocardia. The heart seemed normal. The thyroid was normal. Since 1901 he has had repeated heart attacks and diabetes has been manifest. In a man of 47, who for many years had had symptoms closely resembling stenocardia, there was aréophagia and copious defecation with fat feces. He has had diabetes for a year and a half. A man of 55 was observed who has had diabetes for 3 years. Ten years ago he had all the symptoms of heart neurosis. During his attacks the feces often contained large quantities of fat. There was no goiter. A positive reaction to Loewy's eye test was obtained once. After observations of these patients the author noted carefully the function of the pancreas in subjects with heart neurosis and found that 3 of his patients showed all of the symptoms of disturbed pancreatic function. In one case there was glycosuria; the 2 other patients showed a disturbance of the internal secretion of the pancreas. This raises the question of whether there is a relation between the pancreas and the heart, as there is between the thyroid and the heart. From some cases reported this seems very probable. Also observation of many patients with forme fruste of Graves' disease and with nervous diarrheas may lead us to believe that there is a pathogenetic relation between these symptoms and the pancreas.—J. K.

(DIABETES) Glycemia and hunger (*La glucemia y el hambre local*). Pi Suñer (A.), *Med. ibera* (Madrid), 1921, 15, 103-107.

DIABETES and pregnancy (*Diabete pancreatico e gravidanza*). Piti-mada (F. A.), *Folia med.* (Napoli), 1923, 9, 129-139.

Pancreas extirpation in the dog exactly reproduces human pancreatic diabetes. This operation does not produce diabetes, however, if done in the last periods of pregnancy on account of the substituting endocrine function of the pancreas of the fetus. In agreement with this are the reports of rare clinical cases in which during the last months of pregnancy the glucose elimination ceases or increases, the origin not being in the pancreas alone.—P. N.

The fate of ILETIN in the body. Poucher (G. W.), Cori (K. F.) & Bowen (B. D.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 521.

A brief note. Fasting and fed animals react differently to iletin; iletin is destroyed or eliminated very slowly in the body. Animals do not develop a tolerance for it. No experiments are reported.—J. C. D.

Two cases of retinitis proliferans of syphilitic and DIABETIC origin. Raia (V. L.), *Am. J. Ophth.* (Chicago), 1922, 5, 946-948; cit., *J. Am. M. Ass.* (Chicago), 1923, 80, 59.

(**DIABETES**) The significance and treatment of glycosuria. Rainy (H.), Tr. Med.-Chir. Soc. Edinb., 1921-22, **101**, 46-48; Edinb. M. J., n. s. **28**.

Clinical phases of **DIABETES MELLITUS**. Raynor (W. J.), Nebraska State M. J. (Norfolk), 1923, **8**, 93-95; cit., J. Am. M. Ass. (Chicago), 1923, **80**, 1342.

Cholesterinemia in **DIABETES**. Remond & Rouzaud, Bull. Acad. de méd. (Par.), 1923, **89**, 60-61; abst., J. Am. M. Ass. (Chicago), 1923, **80**, 878.

Case of **DIABETES MELLITUS**. Riely (L.), J. Oklahoma M. Ass. (Muskogee), 1922, **15**, 26.

A case record of a woman of 52. The diabetes was controlled by diet.—W. J. A.

Increase of hyperopia in **DIABETES**. Roberts (W. H.), Am. J. Ophth. (Chicago), 1923, **6**, 291-295; cit., J. Am. M. Ass. (Chicago), 1923, **80**, 1541.

DIABETES MELLITUS. Rolleston (J. D.) & C. L., Med. Sc. (Lond.), 1923, **7**, 355-365.

An excellent review of some of the more important recent literature.—R. G. H.

Rare paralyses in **DIABETES MELLITUS**. Root (H. F.), Med. Clin. N. Am. (Phila.), 1922, **5**, 1433-1440.

Root, of the New England Deaconess Hospital, reports 3 cases of rare paralysis in diabetes. Two were examples of multiple neuritis complicated by chronic nephritis, and the third of isolated paralysis of the peroneal nerve not associated with the more frequent absence of reflexes and loss of sensation.—Med. Sc., **7**, 358.

The **PANCREATIC** hormone as an activator of certain muscle enzymes (*L'hormone pancréatique comme activateur de certaines enzymes des muscles*). Rosling (E.), Compt. rend. Soc. de biol. (Par.), 1923, **88**, 112-114.—T. C. B.

Insulin treatment of **DIABETES MELLITUS**. Rowe (A. H.), Calif. State J. M. (San Fran.), 1923, **21**, 204-208.

A brief survey of the history of insulin, with reports of the results obtained with this substance in the treatment of 24 cases of diabetes during a period of 4 months. The author concludes that the specific we have in medicine, insulin, is one of the most important discoveries of physiologists and diabetes specialists.

The case of a patient who, after the treatment of **DIABETES** (Los puntos de tratamiento de la diabetes), without albumin or sugar. Salomon (H.), J. de la Asociación Médica de Buenos Aires, 1921, **35**, 245-255 (Sec. de Patología).

de med. int.); see also, *Semana méd.* (Buenos Aires), 1921, 28, 249-251.

DIABETES MELLITUS. Diagnosis and treatment. Schlomovitz (B. H.), Jermain (L. F.) & Schuster (B. L.), *Wisconsin M. J.* (Milwaukee), 1923, 21, 355-362; cit., *J. Am. M. Ass.* (Chicago), 1923, 80, 726.

The concentration of sugar in the blood of the rabbit during inanition and after the ingestion of glucose. Scott (E. L.) & Ford (T. H.), *Am. J. Physiol.* (Balt.), 1923, 63, 520-534.—T. C. B.

Etiology and objective symptoms of the liver in 497 cases of **DIABETES** (*Etiologie et signes objectifs du foie de 497 cas de diabète sucré*). Sérégé (H.), *Gaz. hebdomadaire de médecine de Bordeaux*, 1922, 43, 182-187; abst., *Med. Sc.* (Lond.), 1923, 7, 356.

The predilection of diabetes for the male sex is shown by the fact that of Sérégé's 488 patients, 398 were males and 90 females. A history of diabetic heredity was present in 23% of his series. Overeating was a probable cause in 33% of the cases, and alcoholism was incriminated in 9.2%. A history of recent infectious diseases was found in only 14, or 2.8% of Sérégé's cases, the diseases being appendicitis, influenza, and malaria.—R. G. H.

Metabolism in **DIABETES** from the standpoint of antiketogenesis. Shaffer (P. A.), *J. Missouri M. Ass.* (St. Louis), 1922, 19, 134.

Use of **PANCREATIC** extract in **DIABETES**. Sherrington (C. S.), *Nature* (Lond.), 1922, 110, 774; cit., *Chem. Abst.* (Easton, Pa.), 1923, 17, 824.

Glycemia in **DIABETES** (*Studi sulla glicemia*). Silvestri (S.), *Policlin.* (Roma), 1922, 29, Sez. Med., 362-390.

Silvestri points out that the study of glycemia in diabetes is of great importance, not only for diagnosis, but also for prognosis and treatment. Persistence of a high glycemic concentration with a tendency to a gradual rise of the renal threshold while the patient is on a rational diabetic diet is a grave prognostic, and often indicates the occurrence of complications.—*Med. Sc.*, 7, 361.

Relation between syphilis and **DIABETES MELLITUS**. Smith (J. H.), *Virginia M. Month.* (Richmond), 1923, 49, 662-665.

In a series of 79 cases of diabetes Smith found clear evidence of syphilis in only 2 cases, both with heart lesions, probably also syphilitic.—*J. Am. Ass.*, 80, 1102.

The effect of iletin (**INSULIN**) on the blood sugar content in **ADRENALECTOMIZED** animals. Steward (G. N.) & Rogoff (J. M.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 339-341.

In rabbits with both adrenals removed, iletin acts on the blood sugar just as it does in normal rabbits. In the cat, injections of

iletin do not influence the output of adrenin from the adrenals. The hyperglycemia following pancreatectomy in a dog was not influenced, either by removal of one adrenal and denervation of the other, or by complete extirpation. Iletin acted in the same way in this case whether adrenin was being secreted or not.—J. C. D.

The influence of iletin (INSULIN) on morphine hyperglycemia. Stewart (G. N.) & Rogoff (J. M.), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 341-342.

Morphine hyperglycemia differs from other forms in that the adrenals play a part. Iletin acts on the blood sugar in morphine hyperglycemia in the cat and rabbit, as it does in other cases of increased blood sugar. Suppression of adrenal secretion in a cat did not modify the action of insulin. Insulin modified the usual reaction of cats to morphine. Hyperthermia was absent, the temperature falling steadily as in rabbits and dogs.—J. C. D.

Minor ocular symptoms of DIABETES: presbyopia, hypermetropia, myopia (*Les petits signes oculaires du diabète: presbyties, hypermétropie, myopie*). Terrien (F.), *Paris méd.*, 1921, ii, 312-315.

According to Terrien, the ocular complications of diabetes are frequent and various, being met with in more than 10% of the cases in the form of lesions of the cornea, iris, and choroid, cataract, retinal hemorrhages, changes in the optic nerve, amblyopia, affections of the vitreous, ocular palsies, and palpebral and orbital abscesses. In addition to these serious complications are certain ocular symptoms which though of much less gravity are of diagnostic value owing to their frequency and sudden development. Terrien classifies them under the heading of disturbances of refraction and accommodation. Changes in accommodation consist in presbyopia, which occurs at an unusually early age. Of 80 diabetic patients 11, or nearly 14%, presented a diminution of the power of accommodation or, in more marked cases, actual paralysis of accommodation. The changes in refraction consist in hypermetropia, which may develop suddenly without any previous ocular disturbance or, on the other hand, in a transient myopia.—*Med. Sc.*, 7, 359.

(DIABETES) Calcium in the blood. Thro (W. C.) & Elm (Marie), *Proc. Soc. Exper. Biol. & Med.* (N. Y.), 1923, 20, 313-315.

There are two points of direct endocrine interest in this paper. The low carbohydrate diet on which diabetics are placed does not influence the blood calcium in any definite way. In two patients with boils, one of which had low blood calcium, parathyroid therapy was successful.—J. C. D.

Two cases of DIABETES of papular necrotic type (*Due casi di diabete a tipo papulo-necrotico*). Tommasi (L.), *Gior. ital. d. mal. ven.* (Milano), 1921, 62, 477-488.

Relation between DIABETES and syphilis (*Rapports entre le diabète et la syphilis*). Touffet (H.), Thèse de Par., 1922; abst., Presse méd. (Par.), 1922, 30, 1072.

Some authors accord to syphilis a very important rôle in the pathogenesis of diabetes, others, only an exceptional rôle. There are 2 ways of explaining the pathogenesis of syphilis in diabetes: (1) syphilis can cause visceral lesions (hepatic, pancreatic, hypophyseal, thyroid), capable of producing diabetes; and (2) syphilis can cause functional troubles which bring about diabetes. Touffet, in agreement with Labbé, states that syphilitic lesions of the pancreas, liver, etc., found at autopsy in diabetics are very rare. On the other hand, specific treatment has only a slight action on glycogen regulation. Conjugal diabetes, which has been mentioned as an example of syphilitic diabetes, seems to be more dependent upon hyperalimentation than is the case in these subjects. Touffet concludes that it is possible that syphilitic diabetes exists, but that its existence has not been demonstrated. He believes that if there is such a condition it is exceptional.—R. G. H.

Alimentary hyperglycemia and glycosuria with special studies of DIABETES innocens (*Über alimentäre Hyperglycemie und Glykosurie mit besonderer Berücksichtigung der innocenten Glykosurie*). Traugott (C.), Klin. Wchnschr. (Berl.), 1922, 1, 2384; see also, *ibid.*, 2262.

If 20 gm. of glucose followed one hour later by 100 gm. does not cause a rise of blood sugar, it is very probable that the subject does not suffer from real diabetes. Even when this second dose causes a rise it is not certain that the patient has real diabetes.—J. K.

Relation between DIABETES and syphilis. A case of diabetes appearing several days after syphilitic chancre (*Contribution à l'étude des rapports du diabète et de la syphilis. Un cas de diabète sucré apparu quelques jours après un chancre syphilitique*). Villaret (M.) & Blum (P.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, 46, 3 s., 90-94.

The authors, who record an illustrative case in a man aged 45, remark that the relations between diabetes and syphilis have been discussed for the past 50 years, two different opinions being held upon the subject. One school maintains that syphilis is a factor in diabetes by producing nervous lesions, while the other holds that syphilis is merely a debilitating agent without producing any localized lesion. Most of the cases of syphilitic diabetes on record have occurred in the tertiary stage. It is easy to understand how diabetes can be produced by a sclerotic, gummatous, or sclerogummatous process affecting the liver, pancreas, hypophysis, or medulla, or by a meningeal process involving the nerve centres, medulla, or hypophysis. Cases of diabetes are much rarer in the secondary stage, though

examples have been reported by Dub, of Prague, and Sewantie, of Paris. In the present case the diabetes appeared before the chancre had cicatrized, and the symptoms of diabetes developed side by side with those of the syphilitic infection.—Med. Sc., 7, 356.

Tetanus complicating DIABETIC gangrene. Walters (W.), Surg. Gynec. & Obst. (Chicago), 1922, 34, 122 (Jan.).

DIABETES in young persons (Diabetes bei Jugendlichen). Weil-and, Deutsche med. Wchnschr. (Berl.), 1923, 49, 460.

(DIABETES) Discussion on dental sepsis as an etiological factor in disease of other organs. Wilcox (W.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 16 (Sec. Odontology).

Streptococcal and other toxins may lead to toxic glycosuria by impairment of the endocrine function of the pancreas. Accordingly, dental sepsis must always be removed in cases of diabetes, and a rise in carbohydrate tolerance and a disappearance of glycosuria are often observed to follow this procedure.—I. B.

DIABETES MELLITUS. Wilcox (W. H.), Practitioner (Lond.), 1921, 107, 305-321.

A review of the subject from the English physicians' point of view.—J. C. D.

A clinical lecture on DIABETES. Wilder (R. M.), Ann. Clin. Med. (Balt.), 1922, 1, 80-89.

Until recently the author has followed the methods of Joslin and of Allen in the treatment of diabetes. For the last 2 years, however, he has been studying the reactions of diabetics to a high fat diet. Although not ready to draw any positive conclusions he has observed in a number of cases an apparent advantage in the high fat, low protein, moderately low calorie diet recommended by Allen. The urine of patients has become sugar free more quickly, the edema often accompanying starvation has been avoided, better nutrition has been possible and patients have been more comfortable. Charts and formulae for calculating diet are presented and explained.—E. C. A.

Metabolism of DIABETES. Wilder (R. M.), Boothby (W. M.) & Beeler (C.), J. Biol. Chem. (Balt.), 1922, 51, 311-355.

Complete metabolic study of a case of diabetes which terminated fatally. Basal R. Q. averaged 0.693, the highest being 0.74 and the lowest 0.65. Experiments on the immediate effect of food on the metabolic rate and R. Q. showed an unexplained depression of the R. Q., the depression being most marked after large amounts of protein. Basal metabolism was materially affected by the previous diet, being 30% below standard. Raising the food intake to meet the energy requirements raised the basal level; this applies

to under-nourished patients only. Acidosis does not itself raise the basal rate. High basal rate in poorly nourished patients is dangerous. Sugar tolerance is depressed by high caloric diet, more markedly by protein than isocaloric amounts of fat. Glucose tolerance varied adversely as the basal metabolism rate.—Physiol. Abst., 7, 251.

(DIABETES) On the nature of the sugar in blood. Winter (L. B.) & Smith (W.), J. Physiol. (Lond.), 1922, 57, 100-112.

The sugar in the blood of man, and of ox, sheep, cat and rabbit is an unstable form, probably γ glucose. In diabetes it appears to be the α , β form. An enzyme is postulated whereby the α , β form is converted into the γ form. The absence or inactivation of this enzyme is said to be the cause of diabetes.—T. C. B.

The objects and method of diet adjustment in DIABETES. Wood-yatt (R. T.), Tr. Ass. Am. Physicians (Phila.), 1921, 36, 269-292.

See Endocrin., 6, 864.

Surgery and DIABETES. Young (E. L.), Boston M. & S. J., 1923, 188, 767-769.

Not of endocrine interest.—J. C. D.

Salt-poor and salt-free days in DIABETES MELLITUS (Salzarme Diät und salzfreie Tage bei Zuckerkranken). Ziegelroth, Deutsche med. Wchnschr. (Berl.), 1921, 47, 1358.

(ENDOCRINE) Comparable experiments on the action of heated and non-heated bran and yeast and on the organs of pigeons fed with organs of normal pigeons and polished rice (Weitere Beiträge zur Kenntnis von organischen Nahrungsstoffen mit spezifischer Wirkung. XVI. Vergleichende Untersuchungen über die Wirkung von erwärmter und nichterwärmter Kleie und Hefe und ferner von Organen von normal ernährten und von mit geschliffenem Reis ernährten Tauben). Abderhalden (E.), Arch. f. d. ges. Physiol. (Berl.), 1922, 195, 432-459. XVII. Abderhalden (E.) & Wertheimer (E.), *ibid.*, 460-479. XVIII.

In the first paper Abderhalden suggests a division of incretions into two classes, those passing into blood, or lymph circulation, and those manufactured and used in the cells themselves. In the second it is shown that injection of large doses of dl-adrenin leads to a temperature fall lasting some hours, with slower recovery. With doses of 2 mg. the fall is continuous till death some hours later. Gas-exchange, measured by carbon dioxide output, is parallel to the temperature change. Pigeons showing signs of alimentary dystrophy from vitamin deficient food are more susceptible to adrenin action. Adrenin solutions on standing at first show a slight increase in activity; later, a diminution. Animal charcoal completely absorbs adrenin; this can be largely recovered by washing with distilled water. It is not absorbed by kaolin, kieselguhr, nor casein. Talc

reacts, so that after treatment the adrenin gives a deep blue-violet color with ferric chloride, and no longer gives a temperature effect with pigeons.—A. T. C.

The influence of INTERNAL SECRETIONS on the excretion of gastric juice (Zur Frage der Beziehung der inneren zur Sausseren Sekretion. I. Zur Frage ueber den Einfluss der Driisen innerer Sekretion auf der Absonderung des Magensaftes). Alpern (D.), Biochem. Ztschr. (Berl.), 1923, 136, 551-563.

The gastric secretion following the injection of adrenin and pituitrin in dogs was observed. The administration of an amount of adrenin sufficient to produce a typical alteration of the blood pressure had practically no effect upon the first phase of gastric secretion. The slight preliminary retardation was interpreted as a constrictor effect. Pituitrin in doses from 0.025 to 0.075 per kilo caused a marked inhibition of gastric secretion which lasted for 2 or 3 days. Sham feeding was the testing stimulus for the effectiveness of the drugs.—F. S. H.

(ENDOCRINE) The "gastrin" content of the human pyloric mucous membrane. Ammon (S. E.) & Lim (R. K. S.), Brit. J. Exper. Path. (Lond.), 1923, 4, 27; abst., Med. Sc. (Lond.), 1923, 8, 231.

(ENDOCRINE) The principles of rickets (Das Wesen der Rachitis). Aschenheim (E.), Deutsche med. Wchnschr. (Berl.), 1923, 49, 85-86.

After an enumeration of the theories of the patho-genesis of rickets the author discusses his idea that rickets is a pluriglandular disease, the pluriglandular disturbance arising from acidosis, avitaminosis, etc.—J. K.

(ENDOCRINE) Hypercholesterinemia (Uber Hypercholesterinaemie). Barat (I.), Wien. klin. Wchnschr., 1923, 36, 221-223.

There are 2 forms of hypercholesterinemia: the mechanical form and the endocrine form which is caused by increased ovarian activity (pregnancy) or by endocrine disturbances causing diabetes. In diabetes it does not seem to be the diet which causes hypercholesterinemia, but the changed fat metabolism which is always present in severe cases.—J. K.

Chromosomal and INCRETORY hormones (Chromosomale und inkretorische Hormone). Bauer (J.), Med. Klin. (Berl.), 1923, 19, 427-429.

Theoretical consideration of endocrine factors in heredity.
—J. K.

The dermatological symptoms of ENDOCRINE dysfunction. Bechet (P. E.), Arch. Dermat. & Syph. (Chicago), 1921, N. S. 4, 660-670.
A general review.—J. C. D.

(ENDOCRINE) Changes in organ weights of the guinea pig during experimental scurvy. Bessesen (D. H.), *Am. J. Physiol. (Balt.)*, 1923, 63, 245-256.

Twenty-six guinea pigs were divided into 5 groups and fed a scorbutic diet for periods ranging from 5 to 54 days. Animals fed 5, 10 and 15 days appeared normal at autopsy. Those fed for 19 days developed a mild scurvy. Animals fed for 21 to 54 days died of severe scurvy. The sixth group were allowed to develop scurvy and were then cured by a diet of orange juice and green food. In most cases during the first 15 days the changes in weight of the various organs is probably of no significance. After symptoms of scurvy are apparent, changes in organ weight as well as body weight are evident. In comparison with the normal corresponding (final) body weight the ovaries alone appear definitely subnormal. The pancreas (late stage), heart, liver, testes (late stage) and integument indicate a weight roughly proportional to the loss of body weight. The brain, eyeballs, thyroid, spleen and intestines are somewhat above normal, indicating some loss in absolute weight, but less than that of the entire body. The spinal cord, lungs (late stage), kidneys, epididymides, hypophysis (late stage), and urinary bladder are markedly above normal, indicating little or no loss in absolute weight in spite of the great loss in body weight. The suprarenals are increased absolutely as well as relatively. The results show a general agreement with those produced by starvation and tend to confirm the view that changes during scurvy are the result of inanition, although the factors may be different.—T. C. B.

(ENDOCRINE) The nervous and hormone control of the digestive process (*Die nervöse und hormonale Beeinflussung der Verdauungstätigkeit*). Biedl (A.), *Wien. med. Wchnschr.*, 1922, 72, 885-889; 935-939; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1922, 15, 247.

Hunger and thirst sensations are not aroused by the nerves but by blood stimulation on the cerebral cortex, therefore by humoral method. Hormones appear to play an important rôle. Hypophyseal extract has a thirst quenching effect not only in diabetes insipidus, but also in the edema of renal disease. A minimum amount of a certain hormone administered intravenously produces a typical objective picture of hunger—secretory stimulation of digestive juices, increase in muscle tonus and contractions of the digestive tract. Stomach, pancreas and gall secretions are under nervous and hormone control. Pituitrin sometimes produces vomiting. Ovarian extract inhibits vomiting partially or entirely, depending upon the causative factor; this is in accordance with the observation made by Hofbauer regarding vomiting in pregnancy. The tonus of the stomach and intestine is kept up by the autochthonous tonic condition, by the equilibrium of antagonistic innervations and by hormone

influence. Pressure on the cervical vagus produces in some subjects significant effects on the stomach, which can be noted by the roentgen screen; these effects appear in the form of increased tonus, strengthened peristalsis and heaping up of the pylorus opening. Thyroid extract and hypophyseal extract stimulate intestinal peristalsis, while *adrenalin* has the opposite effect. In a nerve trunk impulses may be flowing which produce antagonistic effects, from which a fourfold nervous control results. According to recent experimentation no sharp distinction can be made between innervation and hormone activities.—R. G. H.

(ENDOCRINE) Recent views of some ductless glands. Blackford (C. M.), Virginia M. Month. (Richmond), 1922, 49, 425-430 (November); cit., J. Am. M. Ass. (Chicago), 1922, 79, 2036.

(ENDOCRINE) Thickening of the skin, especially the dorsal skin of the small joints, caused by pluriglandular insufficiency (Hautver dickungen, besonders an der Dorsalseite der Kleinen Gelenke infolge pluriglandulärer Insuffizienz). Blome, München. med. Wehnschr., 1922, 69, 1136.

The patient had a small thyroid and small testes; the prostate had atrophied. He had all the symptoms of hypophyseal gigantism. The Abherhalden's reaction was positive with the hypophysis, thyroid and testes. The skin was thick. Histological examination showed infiltration with small lymphocytes and broad lymph spaces. The skin changes were temporarily improved by injections of "horminum masculinum."—J. K.

The ENDOCRINE factors in some common functional diseases. Blumgarten (A. S.), Med. Clin. N. Am. (Phila.), 1921-22, 5, 1023-1066.

See Endocrin. 6, 811-832.

ENDOCRINES. Box (W. C.), J. Florida M. Ass. (St. Augustine), 1923, 9, 164; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1807.

The reaction of the ENDOCRINE system of the rabbit to tumor inoculation and the relation of this reaction to malignancy. Brown (W. H.) & Pearce (Louise), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1923, 20, 472-476.

The thyroid, parathyroid, suprarenals, hypophysis, thymus, and pineal were observed. All these organs except the last showed changes in size and gross appearance, though alterations in the parathyroids and hypophysis were slight. The thyroid, thymus, and hypophysis showed histological changes. The alterations in weight and histology varied with the stage and severity of the tumor invasion. The ability of the thymus to increase in weight seemed directly related to the ability of the animal to check the tumor. The

seasonal increases in malignancy of the tumor coincided with the periods of endocrine readjustment.—J. C. D.

Animal resistance and the ENDOCRINE system of the rabbit in experimental syphilis. Brown (W.) & Pearce (Louise), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1923, 20, 476-480.

The authors noted changes in the weight of the endocrine organs, notably the adrenals, hypophysis, thyroids, parathyroids, and thymus, together with histological changes particularly noticeable in the last three. Apparently mercury and iodine work through these organs and the actual response of the animal to the disease is determined by the condition of the endocrine system.—J. C. D.

Effects of operative interference with the ENDOCRINES on the growth and malignancy of a transplanted tumor of the rabbit. Brown (W. H.), Pearce (Louise) & Van Allen (C. M.), Tr. Ass. Am. Physicians (Phila.), 1923, May 1-2.

A tumor arising on the site of an old syphilitic lesion on the scrotum of a rabbit was transplanted and followed through 20 generations, and the pathologic reactions following inoculation were studied. This was of interest because of possible relationship of tumors following syphilitic lesions of the mouth. The experimental animals were matched in regard to size and age. Observations on growth, malignancy and metastases of the tumors were made and tested at necropsy. Different groups of experiments were done to note the effect of removal of thyroid, suprarenals, spleen and thymus, respectively, on the tumor, and a fourth group without endocrine interference was used as a control. Operations were designed to interfere with the function of the organ, but to leave the animal in good condition. Operative procedures were carried out both before and after inoculation of the rabbits. We found that in the thyroidectomized animals the tumor grows steadily and rapidly. With the thymus removed, the tumor grows slowly, as in old animals. With partial thyroidectomy, the tumor at first grows rapidly but is brought under control. With complete thyroidectomy, very widespread metastases occurred in all cases; that is, this operation increased malignancy. A seasonal incidence was noted; namely, that malignancy was low in summer and high in spring. In summer, partial thyroidectomy gave a stronger result. The conclusions were that any operation disturbing the animal economy will disturb the resistance of the animal. This work seems to be in line with that of Dr. Murphy on the lymph structures, and is probably part of the same body mechanism.—J. Am. M. Ass., 80, 1954.

The influence of thallium upon the ENDOCRINE system (Experimentelle Beobachtungen über Beeinflussung des endokrinen Sys-

tems durch Thallium). Buschke (A.) & Peiser (B.), *Med. Klin. (Berl.)*, 1922, 18, 731-732.

See *Endocrin.*, 6, 686.

(**ENDOCRINE**) Four cases of muscular dystrophy. Byard (D. S.), *Internat. Clin. (Phila.)*, 1923, 1, S. 33, 174-177.

A report of 4 cases of muscular dystrophy in children aged 5, 6, 9 and 13 years, respectively, all males. The author concludes by stating that there is little known regarding the etiology of the disease, and that "a presumption of endocrine disturbance seems plausible."—I. B.

(**ENDOCRINE**) Monosymptomatic glandular dystrophia (*Distrofie ghiandolari e particolarmente distrofie monosintomatiche*). Campanacci (D.), *Riv. crit. di clin. med. (Firenze)*, 1922, 23, 69, 79, 92.

(**ENDOCRINE**) Opothherapeutic value of milk (*Le lait naturel aliment opothérapique*). Cassoute, *Acad. de méd. (Par.)*, 1922, (December 12); *abst., Presse méd. (Par.)*, 1922, 30, 1088.

The author believes that its hormone content is an important factor in rendering milk a uniquely valuable food.—R. G. H.

(**ENDOCRINE**) Gigantism and dwarfism among animals (*Gigantisme et nanisme dans la série animale*). Chapellier, *Soc. de pathol. comparée*, 1923, March 15; *abst., Presse méd. (Par.)*, 1923, 31, 295.

The author shows that giants and dwarfs, in the medical sense of the word, are extremely rare, if existent, among animals. There are human beings very much below or above the average height, but who are normally constituted. Small wild animals are often found, their size almost always being due to malnutrition or to insufficient nourishment when they were young (rabbits from the islands of Manche). There is also sexual dwarfism, the males being ordinarily smaller than the females; sometimes, however, the male is larger (*diurnal Raptores, Otaria*).—R. G. H.

(**ENDOCRINE**) The syndromes of pluriglandular insufficiency in the adult (*Les syndromes d'insuffisance pluriglandulaire de l'adulte*). Claude (H.) & Sourdel (M.), *J. méd. franç. (Par.)*, 1921, 10, 462-466.

—A generalized diffuse review not amenable to abstracting.

—F. S. H.

ENDOCRINE basis of otorhinolaryngological affections (*Afecciones otorrinolaringológicas y glándulas endocrínicas*). Correa (J. de la C.) & Becco (R.), *Semana méd. (Buenos Aires)*, 1923, 30, 112-117.

A general review. A description is given of several cases ameliorated by opotherapy.—B. A. H.

(ENDOCRINE) The influence of feeding iodized tissues of invertebrates on larvae of *Bufo vulgaris* (Sull'influenza della nutrizione con tessuti iodati d'invertebrati sulle larve di *Bufo vulgaris*). Cotronei (G.), Atti d. r. accad. naz. Lincei, Rendiconti, 1921, 30, 149-151; abst., Ber. ü. d. ges. physiol. (Berl.), 1922, 15, 106.

Giacomini in 1918 reported that iodized spleen causes just as rapid metamorphosis of the frog as thyroid gland preparation. The author performed similar experiments with muscle of invertebrate animals (*Squilla mantis* and *Donax venustus*). He placed the musculature of these animals into a solution of 2 gr. potassium iodide, 1 gr. iodine and 100 gr. water for 24 hours. The muscles thus prepared were washed and fed to the larvae of *Bufo vulgaris*. The metamorphosis was hastened in the same manner as if iodized muscle of vertebrates or thyroid gland had been given; the muscle of crayfish seemed to have a slower effect than that of the mussel. Cotronei, however, feels that he is not justified in drawing further conclusions from these facts without more experimentation.

—R. G. H.

Hyperchlorhydria—a manifestation of ENDOCRINE abnormality. Drummond (J.), South African M. J. (Capetown), 1923, 31, 34-37; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1032.

(ENDOCRINE) Organotherapy of malignant disease. Engel (D.), Ztschr. f. Krebsforsch. (Berl.), 1923, 19, 339-381; abst., J. Am. M. Ass. (Chicago), 1923, 80, 1349.

Partly from a study of the literature and partly from animal experiments with optones Engel concludes that the pituitary seems to promote tumor growth, while the thyroid, and above all the thymus, check it. The elements responsible for this action seem to be the protein products in far advanced retrograde metabolism. Testes and ovaries were found inert. Ovariectomy in inoperable cancer of the mamma is justified by the stimulation of the thymus that results.—R. G. H.

Epilepsy of ENDOCRINE origin (Epilepsie d'origine endocrinienne: essai d'une pathogénie à point de départ cortical). Etienne (G.) & Richard (G.), Rev. méd. de l'est (Nancy), 1922, 50, 308-314; abst., Presse méd. (Par.), 1922, 30, 935.

The authors report a case of late epilepsy which seemed to appear in the course of an endocrine syndrome, notably characterized by hypothyroidism and testicular atrophy. Reports of association between epilepsy and certain genital conditions in women are very frequent. For example, epilepsy is alleviated or disappears during pregnancy. The authors observed a young girl who became epileptic regularly on the first day of each menstrual period, never at other times. In a late epileptic patient, with a pluriglandular syndrome, thyro-ovarian opotherapy deferred the attack, which reappeared at

the time of menstruation when treatment was stopped. In this patient, after prolonged compression of the forearm in the oscilometer, the radial pulse was no longer perceptible in the finger. The subject presented sympathicotonic reactions and was not affected by pilocarpin. Epilepsy is of vascular origin. The authors believe that in certain endocrine conditions there exists a hypertonicity of sympathetic origin of the small arteries of muscular type, such as the cerebral arteries, and that when there is an exacerbation of sympathetic disturbance there is an exacerbation of spasm, the blood suddenly leaves the brain, the conscious sensitive-motor centers of the cortex are more or less totally inhibited and the lower thalamic centers freed. The epileptic attack follows. Another evidence of this mechanism is seen in the epileptic attacks of Stokes-Adams' disease. Munier has studied the rôle of equilibrium of the vago-sympathetic system in disorders of this kind.—R. G. H.

Mental disease of ENDOCRINE origin (Las endocrinopsicopatías).

Fernández-Victorio (A.), *Siglo méd.* (Madrid), 1923, 71, 201-203.

The author relates that a youth of good family and a brilliant student suddenly lost interest in his studies and family and developed a paranoid schizophrenic state. A tendency to adiposogenital dystrophía was pronounced and the young man was abnormally tall. This suggested that the pituitary was responsible for the endocrinopsychopathy, but pituitary treatment alone and thyroid treatment alone failed to benefit. Under mixed organotherapy, marked improvement was realized.—J. Am. M. Ass., 80, 1654.

Relation of INCRETIONS to the origin of skeletal variations (Beziehungen der inneren Sekretion zur Genese einiger im Röntgenbilde praktisch wichtiger Skelettvarietäten). Fischer (H.), *Fortschr. a. d. Geb. d. Röntgenstrahlen* (Hamb.), 1922, 20, 51-56; *abst.*, *Ber. ü. d. ges. Physiol.* (Berl.), 1922, 14, 384.

In some cases of early eunuchoidism puberty appears rather late and is short lasting. In subjects of this type is found a disproportionate skeleton which is characteristic of early eunuchoidism, but which never occurs in cases of late eunuchoidism or of late castration. The author makes a distinction between eunuchoidism and hypogenitalism; in the latter anomaly there is a rather protracted immaturity in the epiphyseal structure, but no disproportion of the skeleton. The increased height in eunuchoidism is the result of stimulation of the anterior lobe of the hypophysis—recognized by the increase in number of eosinophilic cells. This appears as a result of castration. The author accepts as a probable theory that the compact islands sometimes found in the ossifying parts in the region of the epiphyses can be traced to a disturbed functioning of the sexual glands. The possibility is also discussed that the espe-

cially overdeveloped carpals and tarsals in arthritis might be the result of a disturbed function of the hypophysis.—R. G. H.

Pathology of the ENDOCRINE glands of the uterus. Tumors of the incretory glands of the uterus (*La pathologie de la glande à sécrétion interne de l'utérus. Les tumeurs de la glande à sécrétion interne de l'utérus*). Fornero (A.), *Arch. Ital. de biol. (Pisa)*, 1922, 71, 22-39; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1923, 18, 372.

The action of various extracts of ENDOCRINE organs and of various alkaloids on the dilatation of the pupil in the rabbit and frog (*Azione di alcuni estratti di ghiandole endocrine e di alcuni alcaloidi sull'ampiezza della pupilla del coniglio e della rana*). Fracassi (G.), *Arch. di ottal.*, 1921, 28, 154-178, 179-203; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1923, 16, 511.

Ocular manifestations of INTERNAL SECRETION. Fuchs (E.), *Proc. Inst. Med. (Chicago)*, 1923, 4, 73-84.

A somewhat speculative general article not amenable to abstracting.—R. G. H.

ENDOCRINE glands. Fulton (F. T.), *Rhode Island M. J. (Providence)*, 1922, 5, 347-352; cit., *J. Am. M. Ass. (Chicago)*, 1923, 80, 62.

Senescence and ENDOCRINOLOGY. [*Sénescence et endocrinologie. (A propos de la communication de M. Marinesco sur l'opération de Steinach)*]. Gley (E.), *Bull. Acad. de méd. (Par.)*, 1922, 87, 285-291 (March 14).

A critique, pointing out the fact that the ideas of, and operations directed toward, rejuvenescence are by no means new.

—R. G. H.

Changes of blood sugar caused by drugs (*Über die Pharmacologische Beeinflussung des Blutzuckers*). Grossman (M.) & Sandoz (J.), *Wien. Arch. f. inn. Med.*, 1923, 5, 419-428.

The authors found that while atropin diminished the blood sugar in some subjects it had no influence in others. It had no effect in 2 patients with Graves' disease, both of whom were very sensitive to adrenalin and showed the classical type of the sympathicotonic form of exophthalmic goiter. No reaction was seen in 2 patients with diabetes; 1 of them showed only a slight reaction after the injection of adrenalin; in the other, although adrenalin had a slight influence on blood sugar and blood pressure, there was much less of a reaction than might be expected. In other cases of diabetes atropin markedly decreased blood sugar. All of these patients had extremely severe juvenile types of diabetes with very high blood sugar and marked acidosis. The atropin reaction was also seen in a

diabetic with sclerosis of the kidneys in whom adrenalin caused no change in blood sugar but had a very strong influence on the blood vessels. When adrenalin decreases the blood sugar, the reaction is only temporary and is followed the next day by a slight rise. It would therefore be inadvisable to recommend atropin in treatment of diabetes. It is difficult to explain this reaction caused by adrenin and many experiments and pharmacological observations will be necessary before the influence of atropin on metabolism is understood.—J. K.

(ENDOCRINE) *L'organoterapia röntgenologica*. Guarini (C.), *Rassegna internaz. di clin. e terap.* (Napoli), 1922, 3, 491-495.

A brief review without bibliography.—R. G. H.

Various phases of ENDOCRINE conditions. Haley (Y. W.), J. Tenn. M. Ass. (Nashville), 1923, 15, 409-412; cit., J. Am. M. Ass. (Chicago), 1923, 80, 726.

(ENDOCRINE) A case of pluriglandular insufficiency. Harvey (A. D.), *Indian M. Gaz.* (Calcutta), 1922, 57, 100.

(ENDOCRINE) The amount of calcium in human blood serum (*Klinische Untersuchungen über den Kalkspiegel des menschlichen Blutserums*). Herzfeld (E.) & Lubowski (H.), *Deutsche med. Wchnschr.* (Berl.), 1923, 49, 603-605, 638-639.

The amount of calcium in the serum is very constant and variations in abnormal persons are not so rare as many believe. The authors found hypocalcemia (less than 11 mg. % Ca) in aortic aneurysm of syphilis (1 case), ulcer of the stomach (2 cases), tuberculosis of the lungs, etc., and in Graves' disease (1 case). Hypercalcemia (over 11 mg. % Ca) was found in different diseases, among others, 1 case of rachitis tarda combined with hyperthyroidism and 1 case of heart disease due to goiter.—J. K.

The ENDOCRINE system in infancy and early childhood. Hill (O. W.), *South. M. J.* (Birmingham), 1921, 14, 689-696.

A review without new facts.—J. C. D.

(ENDOCRINE) Pluriglandular syndromes, their pathogenesis and their pathological anatomical basis (*Über eigentümliche Verlaufsformen polyglandulärer Syndrome, ihre Aetiologie und ihre pathologisch-anatomischen Grundlagen*). Hirsch (S.), *Deutsches Arch. f. klin. Med.* (Leipz.), 1922, 140, 323-341.

The case is reported of a waiter of 55 who, 11 years before, began to lose his hair. He first lost the power of erection and then his sexual desires. He suffered with obstipation. His skin was cold and without perspiration. His thyroid could be felt. The testicles were about the size of a bean. The skiagram showed a sella turcica with vague borderlines. Injection of adrenalin did not

produce perspiration. He died of broncho-pneumonia. A post-mortem examination was made. The hypophysis was small, with growth of connective tissue and atrophy of glandular parenchyma in both lobes. The pineal contained more than the normal amount of calcium. The thyroid weighed 10 gm. but seemed normal otherwise. The parathyroid glands were normal. The adrenals were degenerated and very small. The testicles were without Sertoli's cells. The sperm canals did not possess any epithelia. All the tissue was changed into a fibrous mass, probably due to syphilis. The case is also reported of a young looking man of 68 who, since his youth, had had extremely scanty hair growth on the trunk, face and pubes.

—J. K.

Some recent work on INTERNAL Secretions (*Algunos trabajos recientes sobre secreciones internas*). Hoskins (R. G.), *Semana méd.* (Buenos Aires), 1923, 30, 406-412.

Spanish translation of an article in *Endocrin.*, 6, 621-632.

—B. A. H.

(ENDOCRINE) Scleroderma treated by pluriglandular opotherapy (*Sclérodémie traitée par l'opothérapie polyglandulaire*). Hugel, *Réunion dermatol. de Strasb.*, 1923, Jan. 14; abst., *Presse méd.* (Par.), 1923, 31, 139.

The author reports a case of scleroderma in bands which had previously been treated unsuccessfully by fibrolysin. Pluriglandular opotherapy, however, caused the lesions to disappear almost entirely; only one band, 4-5 cm., remained on the right thigh. Hugel recommends that pluriglandular opotherapy be tried in all cases of scleroderma.—R. G. H.

ENDOCRINE adiposity (*Demonstration von Fällen endokriner Fett-sucht und Magerheit*). Kämmerer & Thannhauser, *Deutsche med. Wchnschr.* (Berl.), 1923, 49, 70.

The following cases are described: (1) a boy of 16 with dystrophia adiposogenitalis, homonymous hemianopsia and enuresis; (2) a boy of 17 with hypophyseal syphilis; (3) a girl of 12 with precocious puberty; (4) two women of 32 and 36 respectively with retarded eunuchoidism; in both of whom after childbirth, adiposity, diabetes insipidus and symptoms of brain stimulation developed; (5) a boy of 10 with cerebral adiposity; and (6) a man of 27 with hypophyseal cachexia which began after a shock in war; he was 168 cc. in height and only 33 kg. in weight.—J. K.

Constitution and surgery, with special regard to the ENDOCRINE glands (*Konstitution und Chirurgie unter spezieller Berücksichtigung der endokrinen Drüsen*). Kocher (A.), *Schweiz. med. Wchnschr.* (Basel), 1923, 53, 223-240.

A critical discussion of constitutional endocrinology. Its length, general nature and wealth of details render it impossible satisfactorily to abstract.—R. G. H.

(ENDOCRINE) Hormone of muscle tissue. Komaroff (S. A.), *Wratschebnoje delo*, 1921, No. 1-6; 11-15; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1922, 13, 231.

Accepting the theory that all cells of an organism produce a hormone, the author investigated the muscle tissue in this respect, and studied its relationship to the functions of glandular mechanisms. The effect of nitrogenous bases of muscle tissue on secretions of intestinal glands of a dog with an intestinal fistula, if injected intravenously or subcutaneously was proven by Thiry-Vella and Glinsky-Pawlow. In 15 experiments on 3 dogs carnosin was found to be a strong stimulant for secretory and motor functions of the intestine. Histidine affected it similarly, although in general in a somewhat weaker manner. Methylguanadine stimulated not only the intestinal secretion, but also secretions of the stomach, salivary glands, pancreas, liver and other glands. The author believes that all secreted material of the muscle tissue reaches the blood and affects the organism as an active hormone in the same manner as adrenalin and other incretions.—R. G. H.

(ENDOCRINE) Some physical properties of blood serum in health and disease (*Over cenige physiche eigenschappen van bloedserum von gezonden en zieken*). Koopman (J.), *Nederl. Tijdschr. v. Geneesk. (Haarlem)*, 1923, 67 (I), 264-275.

Among 800 determinations of the coagulation point of serum some endocrine diseases were included. In diabetes the coagulation point of the serum is normal; in coma or shortly before coma this point may suddenly become much lower. In Graves' disease when the cases are not severe the coagulation point is normal. Extremely low temperatures of coagulation were found in rabbits in which by an iodine-free diet, thyroid degeneration had been produced.

—Author's Abstract.

Neurogynecological diseases and their relation to the ENDOCRINE organs (*Neurogynäkologische Krankheitsbilder in ihren Beziehungen zur inneren Sekretion*). Landeker (A.), *Ztschr. f. ärztl. Fortbild. (Jena)*, 1922, 19, 494-497.

A somewhat uncritical review.—J. K.

(ENDOCRINE) Pathogenesis of spasmophilia (*Pathogenese der Spasmophilie*). Lederer (R.), *Monatschr. f. Kinderh. (Leipz.)*, 1923, 25, 394-409.

Infantile spasmophilia is, according to the author, a constitutional abnormality caused by a primary disturbance of the equilibrium between Na and K ions and Ca and Mg ions, with a marked

increase of Na and K and a decrease of Ca and Mg. The changes in the H ion concentration found in the blood and tissues are secondary, due to toxic amino bases, etc. Whether this disturbed equilibrium is caused by loss of parathyroid function or whether spasmophilia produces changes in other endocrine glands also is unknown.—J. K.

ENDOCRINE disturbances and nitritoid crises. Lévy (G.), Juster & Lafont, *Ann. d. mal. vén. (Par.)*, 1923, 18, 127-132.

The authors found that accidents in arsphenamin injections are more likely to occur in patients with endocrine troubles. Changes in the thyroid gland may occur during treatment. Irregular menstruation, fleeting edemas, other vasomotor disturbances, and endocrine symptoms should put the physician on his guard against arsphenamin accidents. Epinephrin is an excellent remedy against them. Asthenia, fatigue in the morning, and apathy are among the minor signs of insufficiency of the suprarenals.

—J. Am. M. Ass., 80, 1416.

(ENDOCRINE) The question of a gastric hormone. Lim (R. K. S.), *Quart. J. Exper. Physiol. (Lond.)*, 1922, 13, 79-103.

Edkin's observation that pyloric extracts cause gastric secretion, is confirmed. Adrenalin does not inhibit secretion but may delay its outflow from the stomach. Histamine injected intravenously causes gastric secretion. It is concluded that the excitant is not secreted into the blood stream and that the mechanism of secretagogue action is not due to internal secretion.—T. C. B.

(ENDOCRINE) Etiology and pathogenesis of vitiligo (*Etiologie et pathogénie du vitiligo*). Lindberg (K.), *Thèse de Par.*, 1923; *abst.*, *Presse méd. (Par.)*, 1923, 31, 68.

Vitiligo in some conditions is considered as due to disturbance in the sympathetic system or in the incretory glands—for instance, Graves' disease. The appearance of vitiligo in several nervous affections can also be explained as a sympathetic or endocrine-sympathetic disturbance.—R. G. H.

(ENDOCRINE) Sugar tolerance in dementia praecox and other mental disorders. Lorenz (W. E.), *Arch. Neurol. & Psychiat. (Chicago)*, 1922, 8, 184-196.

Except in cases of active catatonia, certain cases of simple deteriorating dementia praecox and several cases in which evident emotional upsets existed at the time of the test, this investigation points to a blood sugar concentration in mental disease that is practically normal when the test is made while the patient is fasting, the average being 0.105%. Patients with the catatonic type of dementia praecox respond to glucose feeding with a hyperglycemia that resembles the response obtained in hyperthyroidism. Several cases of simple deteriorating dementia praecox responded to glucose feed-

ing in a manner that resembles the responses obtained in certain endocrine disturbances, such as **dyspituitarism**. In the depressed phase of manic-depressive insanity the curve was higher than found in normal subjects.—C. E. N.

The INTERNAL SECRETIONS as an etiologial therapy in the dermatoses of puberty and the climacteric (*Die Beeinflussung der inneren Sekretion als ätiologische Therapie bei Dermatosen der Pubertät und des Klimakteriums*). Luithlen (F.), Med. Klin. (Berl.), 1921, 17, 217-220.

The author's success with thyroid therapy in the treatment of a case of seborrhea, comedo and acne juvenilis in a boy of 17, led him to try organotherapy, usually combined organotherapy with colloid therapy, in skin disorders at puberty and the menopause. Among the cases successfully treated were pruritus universalis in a woman of 62 (ovarian extracts), pruritus vulvae in a woman of 47 (ovarian extracts), furunculosis in a woman of 24 (colloid therapy alone), eczema acneiforme (colloid therapy), acne conglobata in a woman of 24 (colloid and pituitary therapy), acne rosacea in a woman of 48 (colloid and ovarian extract), etc. The author discusses the relation of the skin to the various incretory glands, although the treatment he advises, as would appear in the case reports, is obviously at least semi-empiric.—E. N.

(ENDOCRINE) DUCTLESS GLANDS and their relation to vital phenomena. Mackay (A. W.), Dominion Dent. J. (Toronto), 1921, 33, 297-302.

(ENDOCRINE) Basal metabolism. Marañon (G.) & Carrasco (E.), Ann. de méd. (Par.), 1923, 13, 124-147.

Marañon and Carrasco find a distinct diagnostic and prognostic value in determination of basal metabolism only in affections of the thyroid. It usually allows the differentiation of them from pathologic states grouped under the heading of "pseudohyperthyroid vegetative neuroses." Sex glands and the pituitary act in the same sense as the thyroid. If the disturbances of their function are associated with hypothyroidism or hyperthyroidism, the influence of the thyroid changes prevails, even if the other glands are affected in the opposite sense.—J. Am. M. Ass., 80, 1545.

A new kind of INTERNAL SECRETION: neurocrinology (*Sur un nouveau mode de sécrétion interne: la neurocrinie*). Masson (P.) & Berger (L.), Compt. rend. Acad. d. sc. (Par.), 1923, 176, 1748-1750.

A further addition to the terminology—a subdivision of "neurocrine glands" and "neurohormones" in which the interstitial cells are particularly considered.—A. T. C.

Developmental hypoplasia in children with especial reference to ENDOCRINE dysfunction. McCready (E. B.), Arch. Pediat. (N. Y.), 1923, 40, 287-306.

The author attempts to show that practically all disorders, functional and organic, have constitutional inferiority as the most important etiological factor and that even in the presence of some of the exciting factors the state of constitutional and organic integrity is the factor which determines severity and limitation. The cells of the endocrine system, imperfectly energized, fail to function to normal capacity and the ensuing deficiency in hormonal stimulation of important structures results in further defective development. McCready agrees with Sajous that the treatment of endocrine insufficiencies in the mother is one of the important measures in the prophylaxis of the hypoplasia originating or accentuated during the gestational period.—M. B. G.

ENDOCRINE organs and the vegetative nervous system in children's diseases (Endokrines System und vegetatives Nervensystem in der Klinik der Kinderkrankheiten). Mensi (E.), Monatschr. f. Kinderh. (Leipz.), 1923, 25, 440-453.

A pharmacological study of children proved that though there are a few cases of either vagotonia or sympathicotonia, most cases show symptoms of both. Vagotonia was seen in a case of Graves' disease, 1 case of myxedema, 2 cases of idiocy and 3 cases of diabetes insipidus.—J. K.

The ENDOCRINE glands (Las glándulas endocrinas e de secreción interna). Molina (R. D.), Rev. Filipina de med. y farm. (Manila), 1921, 12, 221, 261.

(ENDOCRINE) Discussion on "the present position of organotherapy." Murray (G. R.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 14-17 (Sec. Therap. & Pharmacol.).

This paper is one of a series constituting a symposium on the present day tendencies in organotherapy. Thyroid substance is a specific in the various forms of frank thyroid deficiency. It is also useful in chilblains (especially if combined with calcium), in some menstrual disorders, nocturnal enuresis, tertiary syphilis, some skin lesions, and in certain forms of constipation. The parathyroid glands are concerned in calcium metabolism and perhaps in the stimulation of leucocytosis especially during septic conditions. Parathyroid may therefore be administered during infections in doses of 1/10 gr. of dried gland by mouth. The suprarenal glands present many problems. Substitution therapy with suprarenal substance in Addison's disease is incapable of permanent results. Nevertheless the value of adrenalin in various conditions in medicine such as hemorrhage, shock, asthma, and in esophageal spasm, is striking. Pituitary, too, cannot be employed in substitution therapy, but the action of pitui-

trin subcutaneously as a stimulant of involuntary muscle fibers is marked. In sluggish uterine contractions in obstetrics, in functional distension of the bowels, and as a cardiac stimulant in such acute conditions as pneumonia, pituitrin is of signal service. Gonadal preparations are of doubtful value in therapeutics. Though removal of the testicles and of the ovaries result in conditions commonly regarded as due to absence of internal secretion of the gonads, there is no definite evidence to prove that eunuchoidism can be overcome by testicular extract or that post-operative menopause can be averted by taking ovarian tablets. The discovery of insulin in the study of pancreatic opotherapy leads us to hope that further researches may yield new and useful information in the field of organotherapy. In preparations of the thyroid, parathyroid, pancreas, suprarenal and pituitary, we have agents of proved value. In the case of the other endocrine glands, while recognizing the importance of their functions, we cannot fairly claim that we know as yet how to obtain or employ active preparations made from them. The recent exploitation of organotherapy for all kinds of diseases is deplorable, as it tends to discredit a valuable means of treatment when properly employed.

—I. B.

(ENDOCRINE) An epidemic of osteomalacia in "Klein-Polen" in the years 1918-20. Orzechowski (K.), Abhandl. polnisch. Akad. d. Wissensch. (Warschau), 1922, 1, 314-360.

The author observed, in the period 1918-20, 93 cases of osteomalacia; 10 of these subjects were men, the others women. Orzechowski does not believe that starvation plays a rôle in the pathogenesis of osteomalacia; on the contrary, these patients may be overfed. It is not the amount of food ingested, the author states, but its composition that is important. Especially vegetable food with little or no fat and meat may cause osteomalacia. The following classification is proposed: (1) alimentary osteomalacia; (2) osteomalacia due to pregnancy; (3) osteomalacia due to or during lactation; (4) osteomalacia due to the menopause; (5) senile osteomalacia; and (6) osteomalacia in which no apparent cause can be detected. Though many investigators deny the identity of endemic and sporadic osteomalacia, Orzechowski believes that all these forms are identical. Osteomalacia is found only in patients of a certain disposition, depending largely on the relations between the different parts of the involuntary nervous system, and these patients become ill, the author thinks, when they are infected with the osteomalacia virus. As this is a typical pluriglandular disease, it is stated that the osteomalacia virus has a special affinity towards the hypophysis, the parathyroids (as a certain relation between tetany and osteomalacia seems to exist) and the sex glands. As to treatment, phosphorus, especially, may be valuable. Only when this remains unsuccessful

is castration advocated. Of his 93 cases, ablation of the ovaries was performed only 3 times—in each case with brilliant success.—J. K.

ENDOCRINOLOGY and psychology. The endocrine sympathetic system according to the modern analysis of human personality. II. The endocrine sympathetic factors in personality (*Endocrinologia e psicologia. Il sistema endocrino-simpatico nell'analisi moderna della personalità umana. II. Il determinismo endocrino-simpatico della personalità*). Pende (N.), *Quaderni di psichiatria*. (Genova), 1921, 8, 209-228; abst., *Ber. ü. d. ges. Physiol.* (Berl.), 1922, 14, 250-251.

An attempt to classify the endocrine and autonomic factors determining personality.—E. C. A.

ENDOCRINE organs and coagulation of blood. Perrin (M.) & Hanns (A.), *Arch. d. mal. du coeur etc.* (Par.), 1922, 15, 617-640 (September).

Most of the organs have both a coagulating and anti-coagulating action. Perrin found a simple coagulating action in the thymus, spleen, bone marrow and kidney. A similar but much more intense action was manifested by the pituitary, bowel, lung, skin and ovaries. Similar action of the thyroid may be perhaps due to the internal secretion.—J. Am. M. Ass., 70, 2195.

The endocrine influence of the LIVER on diuresis (*Über die hormonale Wirkung der Leber auf die Diurese*). Pick (E. P.) & Wagner (R.), *Wien. med. Wchnschr.*, 1923, 73, 78-82.

Wagner has described (*Ztschr. f. d. ges. exper. Med.*, 1921, 25, 361) the case of a girl of 9 who suffered with tumor of the liver and with symptoms of very marked hypothyroidism. In this child water metabolism was carefully studied. It was severely disturbed. When 250 gm. water was given only 160 gm. was excreted by the kidneys. The excretion of urea was also very low. Since no known function of the liver can explain this symptom, the authors concluded that the liver has an endocrine function regulating the water and urea metabolism.—J. K.

BLOOD SUGAR regulation (*Beitrag zum Studium der Blutzuckerregulation*). Pollak (L.) & Wagner (R.), *Med. Klin.* (Berl.), 1923, 19, 430-432.

Wagner reported (*Biochem. Ztschr.*, 1922, 127, 55) the case of a girl of 10 years with a tumor of the liver and pluriglandular disturbances. Blood sugar on the empty stomach was exceedingly low. After administration of sugar there was marked and long lasting hyperglycemia with glycosuria. When proteins were given the blood sugar became normal or slightly subnormal. Ingestion of fat had no influence on the blood sugar. When adrenalin was injected the sugar remained unaltered also. When thyroidin was given the

blood sugar increased gradually up to normal. This child had the appearance of a patient with diabetes. From investigations of sugar metabolism in this patient the authors concluded that the intensity of alimentary hyperglycemia depends upon the rapidity with which sugar is resorbed from the bowels into the blood, and the quantity of endogenous sugar present in the blood and in the liver. After ingestion of a quantity of glucose, repeated later, typical blood sugar tracings are observed. In healthy persons a second dose does not produce a second rise. The tissues (liver, blood) can eliminate sugar quickly when they have already been stimulated by a previous dose; but it is also possible that after a second dose of sugar the liver retains this substance and does not give it off to the blood the second time. Staub has formulated a new theory to explain this fact. He believes that after repeated administration of sugar the liver produces more enzymes to build up glycogen or to oxidize sugar. Pollak and Wagner, however, have advanced another theory in explanation of the fact that a second dose of sugar does not produce a second rise of blood sugar, namely, that the first dose of sugar produces a decreased production of sugar by the liver. This theory explains the metabolic changes in the patient above mentioned. On the empty stomach the patient has but a small quantity of sugar in the blood and therefore the liver gives only very little sugar to the blood.—J. K.

Effects of ENDOCRINE disorders in obstetrics (*Les endocrinopathies dans leurs rapports avec l'obstétrique*). Ramos (A. P.) & Perez (M. L.), *Rev. españ. de obst. y ginec.*, 1922 (April); *abst., Rev. franç. de gynéc. et d'obst. (Par.)*, 1923, 18, 62 (Jan.)

DUCTLESS GLANDS in relation to certain dermatoses. Ravitch (M. L.), *Illinois M. J. (Oak Park)*, 1923, 43, 201-203; *cit., J. Am. M. Ass. (Chicago)*, 1923, 80, 1099.

Some aspects of ENDOCRINOLOGY. Reed (C. I.), *Kansas M. Soc. J. (Topeka)*, 1923, 23, 65-67; *cit., J. Am. M. Ass. (Chicago)*, 1923, 80, 1270.

(ENDOCRINE) Precocious puberty. Reuben (M. S.) & Manning (G. R.), *Arch. Pediat. (N. Y.)*, 1922, 39, 769-786; *ibid.*, 1923, 40, 27-45.

A review of the literature (about 400 cases) is given. The authors conclude that in a great majority of cases precocious puberty is due to functional hypersecretion of certain glands, and in the minority of cases, to malignant growth in certain of these glands. They have not encountered a single case at autopsy or operation in which a primary dysfunction of the pituitary gland was found; they think, therefore, that the evidence in cases of pituitary precocity is not conclusive. Not a single case of thyroid precocity came to autopsy in which the condition was due primarily to the thyroid.

It may be secondarily involved, however. The glands which can primarily produce permanent sex precocity are the adrenal cortex, pineal and the ovaries and testicles. Precocious puberty is not only a sexual precocity but also a total precocity which involves the whole body and all its organs. It is not a distinct entity. The authors present in detail the symptomatology of the condition as it varies with the gland affected. Eight personal cases are reported.

—M. B. G.

(ENDOCRINE) Behavior disorders in children. Rhein (J. H. W.), Penn. M. J. (Harrisburg), 1923, 26, 388-394.

Of indirect endocrine importance in that occasional types of behavior disorders in children are partially traceable to disturbed function of the organs of internal secretion.—I. B.

ENDOCRINE balance. Sands (M. L.), Missouri State M. Ass. J. (St. Louis), 1923, 20, 24 (January); cit., J. Am. M. Ass. (Chicago), 1923, 80, 507.

(ENDOCRINE) Influence of incertions upon hibernation (Über den Winterschlaf und seine Beeinflussung durch die Extrakte innersekretorischer Drüsen). Schenk (P.), Arch. f. d. ges. Physiol. (Berl.), 1922, 197, 66-80.

The author measured the respiratory exchange of hibernating hedgehogs with a Guerber modification of the Haldane open circuit apparatus. He found that during the period of deepest hibernation the respiratory quotients varied from .41 to .65 and the CO₂ output per kg. per hour varied from 1.449 to 1.484 grams. Subcutaneous injection of extracts, presumably commercial, of the thyroid, thymus, anterior lobe of pituitary and adrenalin caused a marked rise in heat production, often producing complete awakening of the animal, the respiratory quotient rising following the injections as high as .83 in 2 to 3 hours. Extract of the posterior lobe of the pituitary had no effect, likewise testicular extracts (testiglandol) were without effect, while ovarian extracts (ovoglandol) distinctly raised the heat production. The work in general confirms the more extensive studies of Adler. Schenk concludes that hibernation results from a correlated depression of the incertory glands.—D. M.

Interrelations of the glands of the INTERNAL SECRETIONS. Scott (J. T.), J. Kansas M. Soc. (Topeka), 1922, 22, 67-71.

The intrasecretory relationship between some ENDOCRINE glands and the uterus. A combined pathological condition of the uterus (metritis cavernosa), the THYROID and the ADRENALS [Zur Frage der intrasekretorischen Wechselbeziehungen einiger endokrinen Drüsen und des Uterus. Eine Kombinierte Erkrankung des Uterus (Metritis cavernosa) der Schilddrüse und der Neben-

niere]. Serdjukoff (M. G.), Arch. f. Gynäk. (Berl.), 1923, 118, 561-585.

A case report with much speculative discussion.—F. S. H.

Common symptoms of divers ENDOCRINE origin (les symptômes endocriniens communs). Sézary (A.), Presse méd. (Par.), 1922, 30, 1075-1076.

Sézary discusses the need of establishing the cardinal symptoms referable to lesions of each of the endocrine glands through carefully interpreted anatomical and clinical studies. He warns against the indiscriminate acceptance of so-called pluriglandular symptoms, although there is an interaction between the endocrine glands, and lesions of one gland may give rise to disturbances in another. He shows that many basic symptoms of endocrine insufficiency may be of totally different origin. Abnormal pigmentation of the skin, which is commonly considered evidence of suprarenal inadequacy is also found in hepatic disease, in hyperthyroidism, in tumors of the pituitary, and in diseases of the gonads when microscopic examination fails to reveal any lesions of the suprarenal glands. Asthenia and obesity myopathies are common features of many and divers endocrine syndromes. True infantilism may be referable to the thyroid, the hypophysis (Souques and Chauvet) to the gonads (Variot, Gandy, Cordier and Rebattu), to the liver (Gilbert and Fournier), and even to the suprarenals (Morlot). Gigantism may be of hypophyseal or of testicular origin. Macrogenitalism is at times caused by tumors of the suprarenal cortex (Bullock and Sequeira). Virilism and hirsutism result from lesions of the suprarenals (Lannois, Pinard and Gallais), of the ovary (Tuffier, Weil, Plichet, Achard and Tiers), of the pineal (Sicard and Hagueneau), or of the pituitary (Blair Bell). Disturbances of hair growth may be caused by insufficiency of the thyroid or of the testicle. Some symptoms attributed to the endocrine glands may not be referable to these glands at all. Sézary wishes to establish the conception of "common" endocrine symptoms in contrast to pluriglandular symptoms, though the two conceptions do not exclude each other, as both are based on anatomical and clinical findings.—G. L.

ENDOCRINE organs and the intestinal tract (Endokrine Drüsen und Verdauungsapparat). Singer (G.), Wien. klin. Wchnschr., 1923, 36, 273-276.

The influence of the endocrine glands on the intestinal tract is undeniable. As proof of this fact the author mentions the diarrhea in Graves' disease and the atony of the intestines in myxedema. When a. preparations are sometimes useful in cases of intestinal think, therefore glands also are closely associated with the bowels. not conclusive. No very severe disturbances of the bowels are ob- autopsy in which the changes from the bowels which are sometimes

so profuse as to suggest a tumor of the bowels. Ovarian preparations in these cases, however, are often unsuccessful. Singer found that good results may sometimes be obtained with extracts of hypophysis, a gland which affects the bowels as well as the ovary. In men there seems to be a relation between the testes and the bowels, but our knowledge is too insufficient along this line to allow clinical conclusions.—J. K.

(ENDOCRINE) Avitaminosis and experimental lesions of the mesenteric nerves (*Avitaminosi e lesioni sperimentali dei nervi mesenterici*). Spadolini (I.), *Arch. di fisiol.* (Florence), 1922, 20, 165-190.

Among other effects following complete section of the mesenteric nerves in cats were atrophy of the pancreas, which appeared reddish in color, a sclerosed regressive condition of the thyroid, and hypertrophy of the adrenal with fatty degeneration especially of the cortex. The results are compared with conditions in avitaminosis, and are discussed in connection with Findlay's theory (*Biochem. J.*, 15, 104; *J. Path. & Bacteriol.*, 24, 175) that when the tissue content of vitamin B falls below a certain level the phosphorized lipid is immobilized in the adrenal cortex instead of passing to the central nervous system.—A. T. C.

ENDOCRINE factor in electric excitability. Specht (O.), *Beitr. z. klin. Chir.* (Tübing.), 1923, 128, 25-54.

Specht gives 14 pages of tabulated data of extensive experiments on guinea-pigs to determine whether removal of one or several endocrine glands would modify spastic conditions. The experiments were numerous and diverse, but the findings were constantly negative. They do not sustain in any way Brüning's recent suggestion that removal of the suprarenals might favorably affect epilepsy.—*J. Am. M. Ass.*, 80, 1185.

Disorders of ENDOCRINE function. Spencer (J. H.), *J. Roy. Army Med. Corps* (Lond.), 1923, 40, 205-511.

A general review of specific tests.—A. T. C.

The action of ENDOCRINE extracts on blood catalase (*Ueber die Einwirkung von Organextrakten auf die Blutkatalase*). Steppuhn (O.) & Timofejewa (A.), *Biochem. Ztschr.* (Berl.), 1923, 136, 213-223.

Freshly drawn rabbit blood was incubated with extracts of various organs of the same species and the catalase activity determined and compared with controls. It was found that extracts of all the organs had the power to increase the catalase activity of rabbit blood. Among the organs studied were the spleen, liver, adrenals, thymus and thyroid.—F. S. H.

Production of hormones by the ENDOCRINE glands in vitro (*Production d'hormones par les glands endocrines in vitro*). Stern (L.) & Battelli (F.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 573-575.

An attempt was made to ascertain in general whether incretory cells separated from the organism retained the faculty of producing their specific hormones. A method of cultivating the tissue is described, and the results obtained from preliminary experiments with the adrenal medulla show that strips of the gland suspended in the blood of the same species and oxygenated continue to produce adrenalin. The same is true for the spleen and testicle.—T. C. B.

ENDOCRINES in pregnancy. Stone (W. E.), *Kansas M. Soc. J. (Topeka)*, 1922, 22, 304; cit., *J. Am. M. Ass. (Chicago)*, 1922, 79, 1638.

(ENDOCRINE) Clinical value of basal metabolism in infancy and childhood. Talbot (F. B.), *Arch. Pediat. (N. Y.)*, 1922, 39, 419-431.

In the majority of instances the basal metabolism at puberty is normal, but in a few instances it is increased. The elevated metabolism is found only in those children with visibly enlarged thyroids, most commonly in girls, and at times may be as high as 30 plus. Such patients may also show some of the milder signs of toxic goiter but as a rule the symptoms are not severe and they probably represent a temporary hyperthyroidism of puberty. The carbohydrate tolerance in diabetes mellitus is so low that prolonged under feeding is necessary in order to prevent acidosis. Basal metabolism determinations give values slightly less than the minimum number of calories consistent with continued life. The basal metabolism is increased in hyperthyroidism and decreased in hypothyroidism and cretinism. Talbot claims that a diagnosis of the latter condition can be made in very early life by means of basal metabolism determinations. The dosage of thyroid can be controlled by aid of these determinations. Basal metabolism in mongolianism varies. In some cases it is low and indicates that the condition is associated with a hypothyroidism which requires thyroid medication. Backward children with a low basal metabolism should be given thyroid preparations. In cases of association of pituitary and thyroid gland dyscrasias, we must conclude that low basal metabolism means a deficiency of the thyroid as there is no positive evidence that the pituitary gland effects basal metabolism. Basal metabolism determinations are of value in cases of hyperthyroidism treated by x-rays as an indicator of when to discontinue treatment. Their use must be stopped when the basal metabolism is still above normal so as

not to induce hypothyroidism. In toxic goiters there is an increase in basal metabolism while in non-toxic goiters the rate is normal.

—M. B. G.

Insufficient nutrition and ENDOCRINE disturbances (*Unternährung und innere Secretion*). Tallqvist (T. W.), *Acta med. Scand.* (Stockholm), 1922, 56, 640-657.

Not the quality but the insufficient quantity of food is probably the most important factor in the dyscrasic diseases known from the war. The endocrine glands are very sensitive to inanition. Sehrt and Peiser have shown that the people of Central Europe suffered from hypothyroidism and hypoadrenalism during the blockade. Organotherapeutic remedies could not be prepared in Germany because the animals gave very bad preparations. According to the author diseases of an endocrine nature—diabetes mellitus and exophthalmic goitre—have shown a remarkable change in frequency in Finland during this time. In Finland food was scarce during the years 1916-1919, and especially in 1918-1919. The author has found that the frequency of the above mentioned diseases was considerably decreased during this period as compared with the years 1912-1916 and 1919-1922. He has obtained an average body weight for each year by weighing all of his patients. The curve demonstrating the decrease of the body weight during the inanition-period runs parallel with the curves of the diseases mentioned.—H. B.

Visual troubles and disturbances of the glands of INTERNAL SECRETION (*Troubles visuels et altérations des glandes à sécrétion interne*). Terrien (F.), *Arch. d'opht. (Par.)*, 1922, 39, No. 12 (Dec.); *abst., Presse méd. (Par.)*, 1923, 31, 204.

(ENDOCRINE?) Scleroderma in bands with extensive pigmentation (*Sclérodémie en bandes avec pigmentaires multiples*). Thibierge (G.) & Rabut, *Bull. Soc. franç. de dermat et de syph. (Par.)*, 1921, 28, 174-176.

(ENDOCRINE) Internal secretions in their relationship to mental disturbance. Tucker (B. R.), *Am. J. Psychiat. (Balt.)*, 1922, 2, 259-273 (October); *cit., J. Am. M. Ass. (Chicago)*, 1922, 79, 2190.

Pluriglandular ENDOCRINE insufficiency and myositis (*Pluriglanduläre endokrine insuffizienz und Myositis*). Viessmann (A.), *München. med. Wehnschr.*, 1922, 69, 1383-1384.

Case report.—J. K.

(ENDOCRINE) Discussion on "The present position of organotherapy." Vincent (S.), *Proc. Roy. Soc. Med. (Lond.)*, 1923, 16, 10-24 (Sec. Therap. & Pharmacol.).

A discussion on the facts and especially the fallacies of current views on organotherapy. Vincent urges that ultra conservatism is by far a lesser evil than unbounded enthusiasm. An occasional good

result from a given remedy is no ground for its general adoption. The cure cannot be proved to be due to the remedy in question, for suggestion, too, plays its part. We must all endeavor to avoid the ancient *post hoc ergo propter hoc* stumbling block in treatment. Thyroid medication deserves its place in the treatment of thyroid hyposecretion and in some cases of goiter and obesity. Such conditions as rheumatism, rickets, mental disease and epilepsy are occasionally reported to have been benefitted by thyroid opotherapy. This is probably due to a stimulation of the chemical activities of the body and not through any specific, direct influence. Parathyroid medication is of doubtful value. Parathyroid implantation may be of service in tetany, but the oral administration is probably useless. In this connection we must bear in mind that aside from cases due to the actual operative removal of the parathyroids, there is no satisfactory evidence that tetany is due to a lesion of the parathyroid bodies but is a name applied to a condition arising from a great variety of causes. Pituitary medication is rather doubtful in value in so-called pituitary disease. Symptoms formerly attributed to lesions of the pituitary body are in reality probably due to injury to the hypothalamus. Though posterior pituitary preparations are valuable in diabetes insipidus and as an aid in contraction of the uterus, and also in meteorism, these are not instances of "substitution therapy" and have no bearing on the functions of the organ. Adrenal medication is emphasized in the use of adrenin by the profession. "But this value bears a very problematic relation to the function or functions of the adrenal body as a whole, or to the services possibly rendered to the animal economy by the chromophil tissues." This, again, is not substitution therapy. In Addison's disease adrenal substance does not seem to be of the slightest value. Adrenin, given by mouth, does not produce the slightest effect in health or disease, unless perhaps on the mucosa of the stomach. Testicular and ovarian medication, given by mouth, are practically useless. Administered subcutaneously, there may be observed a nonspecific irritation or stimulating effect which may result from the administration of other organs and tissues. Vincent mentions the Steinach and Voronoff operations as procedures of improved merit. With regard to testicle transplantation, he points out that unless blood-vessel suture is employed and material from human beings or anthropoid apes is used, grafting is at best a temporary expedient. Pancreatic medication has not proved to be of any value in the treatment of diabetes. Insulin is still in the experimental stage, but it seems that a step in advance has been made, and possibly we will soon have a substance for diabetic patients comparable in specificity to thyroid extract in myxedema. Finally, the author believes that the only existing instance of substitutional therapy is thyroid administration, but that possibly the pancreas may soon be

included in this category. However, such substances as adrenin and posterior pituitary are valuable drugs, apart altogether from the question of internal secretion. The rest of the gland and tissue preparations do not deserve mention except that their exploitation on the present-day scale constitutes a very formidable kind of quackery. "There is no subject upon which so much utter nonsense has been talked as upon internal secretion, and organotherapy, or at any rate a large part of it, may be defined as the application of this nonsense to practical medicine. In the meantime certain firms of manufacturing druggists are making the most of a unique opportunity and are growing rich by reason of the inadequate education of medical practitioners and the notorious ignorance of the general public on all matters relating to their own bodies."—I. B.

INCRETORY glands and their anatomo-pathological changes in epilepsy (*Ghiandole a secrezione interna e loro alterazione anatomo-pathologiche nella epilepsia*). Vizioli (F.), *Ann. di nevrol. (Napoli)*, 1921, 38, 209-235.

(ENDOCRINE) Ateliotic dwarfism. Weber (F. P.), *Internat. Clin. (Phila.)*, 1921, 31S, 91-96.

A report of two cases of ateliosis, i. e., dwarfism due to incomplete development. In both cases there was retardation of mental development. Though largely due to pituitary involvement, the pathogenesis is probably of pluriglandular origin. The first case described is a male 53 years old, whose height in stocking feet is 47½ inches. At 45, the patient weighed 58 3/10 pounds stripped. His head is slightly oversize, his sexual organs are undeveloped, his voice is high pitched, but the expression, the wrinkled face, the attitude and general behavior are somewhat those of an adult. His mental development is that of the average child of 8. There seem to be some associated evidences of hypothyroidism. The second case is that of a male of 35, who is 51 1/5 inches in height, and weighs 66 pounds. His bodily development is less than that of a boy of 10. His limbs are long in proportion to the trunk, and the head is somewhat large. There is sexual underdevelopment. The history indicates that the patient was normal up to the age of 8, and then ceased to grow. He has never been able to earn a living. His mental development corresponds to that of a boy of 9.—I. B.

(ENDOCRINE) Theory on the hormone rôle of the synovial fluid in regeneration of sinews (*Zur Theorie über die hormonartige Wirkung der Synovia auf die Schnewregeneration*). Wehner (E.), *Zentralbl. f. Chir. (Leipz.)*, 1922, 49, 1467-1468.

Bier has proposed a theory, that in cases in which cut tendons do not show regeneration the synovia produces hormones retarding regeneration. Wehner was never able to show the existence of such substances.—J. K.

(ENDOCRINE) Osteomalacia. White (E. P. C.), Arch. Int. Med. (Chicago), 1922, 30, 620-628.

A discussion of this disease in man, monkeys, other animals and birds; especially its etiology, whether a vitamin deficiency, a metabolic disorder or primarily an endocrine dysfunction.—H. L.

Anaphylactic reactions and the ENDOCRINE glands (Colloïdoclasie et glandes endocrines). Widal (F.), Abrami (P.) & de Gennes (L.), Presse méd. (Par.), 1922, 30, 385-388.

Widal, Abrami and de Gennes show by means of a detailed clinical history and prolonged observations that endocrine anomalies are the substratum on which anaphylactic manifestations develop. A woman, aged 40, had suffered for 26 years from typical attacks of idiopathic asthma, with severe, spasmodic attacks of dyspnea, but without any pathologic changes of the respiratory tract. The attacks were elicited by divers contributory causes, especially by inhalation of the scent or the pollen of roses; the endocrine basis of the attacks could be traced definitely to disturbances of thyroid and ovarian function. They began at the age of 14, simultaneously with menstruation, disappeared temporarily at the age of 23 during pregnancy, returned after delivery, and changed their character completely after the sudden appearance of the menopause at the age of 37. During the climacteric the severe, intermittent attacks of dyspnea gave place to a chronic form of dyspnea. Typical myxedema developed. Although no asthmatic crises had occurred for 3 years the sensitization to the pollen of roses persisted. An attack produced by roses led to a transient immunity; an inhalation of rose scent for 15 minutes later was followed by a much milder attack and a third attempt after another 15 minutes produced no symptoms at all. Blood counts made at intervals of one minute during the attacks revealed a sudden drop of the leucocytes and this leukopenia invariably preceded the attack by a few minutes. Ingestion or hypodermic administration of atropin ($4\frac{1}{4}$ mg. by mouth at one-half hour intervals, 1 mg. subcutaneously) were found to prevent both leukopenia and dyspnea when the roses were smelled 15 minutes after administration; but subcutaneous injection of 1 mg. epinephrin had no effect whatever. The possibility of a so-called "psychic asthma" was excluded experimentally—artificial roses produced no symptoms. Under treatment with thyroid extract in increasing dosage (30 centigrammes daily were given finally) the early morning dyspnea, the sensitization to roses and all the symptoms of myxedema disappeared completely. Attention is called to the striking fact that sensitization to the pollen of roses, an anaphylactic phenomenon, yielded to thyroid medication and to the clinical data concerning the sexual cycle, which justify the assumption that thyroid insufficiency existed long before it became strikingly mani-

fest, and that it played an important part in the anaphylactic reactions.—G. L.

The ENDOCRINE factor in mental disease. Wilson (J. L.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 21-30 (Sec. Psychiat.).

An excellent review of the relationship between body and mind with the endocrine organs as the intermediary. The article does not lend itself to abstracting and should be read in its entirety to be fully appreciated. The author concludes as follows. (1) The gross changes in behavior characteristic of mental disease have not up to the present time been correlated with any definite lesion in the nervous system, therefore it is justifiable to look elsewhere for the underlying cause of mental symptoms. (2) The endocrine glands and their apparently close relationship with the primitive instincts and emotions offer a field of study which may be prolific in results to the alienist as well as to the physiologist. (3) There is evidence that the system of endocrine secretions may be affected pathologically by both psychical and physical causes. (4) The endocrine system may prove to be the mechanism through which mental disease is produced.—I. B.

The action of extracts of ENDOCRINE glands upon motor nerve and muscle. Yoshimoto (M.), Quart. J. Exper. Physiol. (Lond.), 1922, 13, 5-40.

Within the concentration range of 0.1% and 1%, all the endocrine gland extracts produce a slight depression of excitability in frog's nerve. The conductivity of the nerve is not affected. There is very feeble or no effect on muscle.—T. C. B.

The influence of TESTICULAR extracts on some chemical properties of the blood (Ueber den Einfluss des Testikular-Extraktes auf einige chemische Eigenschaften des Blutes). Alpern (D.), Biochem. Ztschr. (Berl.), 1923, 136, 542-550.

(GONADS) Milk secretion in virgins (Contributo allo studio della secrezione lattea nelle vergini). Amistani (E.), Nuovo Ercolani (Torino), 1921, 26, 126-128.

Of little endocrine interest. Breast secretion in a virgin bitch was observed after she had suckled 5 puppies. There was no modification of the reproductive apparatus.—P. N.

Influence of temperature on the action of the TESTICULAR hormone (Influence de la température sur l'action de l'hormone testiculaire). Aron (M.), Compt. rend. Acad. d. sc. (Par.), 1923, 177, 141-143.

Experiments on tritons show that low temperatures permit the prolonged maintenance of sexual characters after castration, while heat accelerates the regression. Since those animals subjected to cold show no signs, even after a long delay, of slowed involution,

but signs of evolution indicating the continuity of action of the hormone, it is concluded that it is the residual hormone itself remaining after castration which is affected by the temperature.

—A. T. C.

(GONADS) Retardation of senility (Steinach's method); its theory and practice. Benjamin (H.), N. Jersey M. Soc. J. (Orange), 1922, **19**, 315-320 (November); cit., J. Am. M. Ass. (Chicago), 1922, **79**, 2034.

(GONADS) Interstitial cells of the TESTICLES of the domestic cock. Evolution and structure (Sur les cellules interstitielles du testicule du coq domestique. Evolution et structure). Benoit (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1382-1384.

Histological.—T. C. B.

(GONADS) A method for measuring the absolute mass of TESTICULAR interstitial tissue (Sur une méthode permettant de mesurer la masse absolue du tissu interstitiel testiculaire). Benoit (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1385-1387.

Technical.—T. C. B.

(GONADS) The quantitative relation between the TESTICULAR interstitial tissue, the seminal tissue and the mass of the body in birds and some mammals (Sur les rapports quantitatifs entre le tissu interstitiel testiculaire, le tissu séminal et la masse du corps chez les oiseaux et quelques mammifères). Benoit (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1387-1390.

Technical.—T. C. B.

(GONADS) The physiological conditions relative to the periodical nuptial adornment of birds (Sur les conditions physiologiques relatives à la parure nuptiale périodique chez les oiseaux). Benoit (J.), Compt. rend. Acad. d. sc. (Par.), 1922, **174**, 701-704.

Study of two tropical species *Pyromelana franciscana* and *Hypochera chalybeata* led to the conclusion that there exists a direct correlation between the state of the testicular interstitial gland and nuptial adornment, and that when the sexual character regresses or is absent these interstitial cells present the morphological characters of almost complete functional repose. There is no such parallelism with the seminiferous tubules.—A. T. C.

Unusual contents of OVARIAN cysts—Report of two cases. Bolt (W.), Canad. M. Ass. J. (Toronto), 1923, **13**, 250-252 (Apr.).

The case is reported of a woman of 61. The observations were made 11 years after the menopause. A large irregular, nodular, abdominal tumor, uterine hemorrhage, free abdominal fluid and marked loss of weight were noted. Examination of the tumor disclosed a dermoid cyst, with the usual contents of hair and teeth

plus "typical normal thyroid tissue." The case is also described of a subject of 35 years, having 5 children. A right-sided movable pelvic tumor was removed. Examination revealed a dermoid cyst; one part on "microscopic section showed cells very like those of the cortical layer of the adrenal gland." Cameron reported that "the dermoid cyst tissue appeared to consist of adrenal, chiefly yellow cortex, with a small dark streak of what appeared to be medulla." One sample was 0.26% adrenalin.—J. H.

(GONADS, HYPOPHYSIS) Drugs and basal metabolism. Boothby (W. M.) and Rowntree (F. G.), *J. Pharmacol. & Exper. Therap.* (Balt.), 1923, 21, 198-99.

The effect on basal metabolism of various drugs including ovarian extract and solution of hypophysis was studied. The authors do not believe the experiments sufficient in number to eliminate the possibility of slight variation in metabolism—up to 5 per cent—but think they do exclude variations of greater magnitude occurring within 90 minutes after administration.—G. E. B.

(GONADS) The effects of castration in relation to age at time of operation. Bormann (F.), *Skandin. Arch. f. Physiol.* (Leipz.), 1922, 42, 240-249.

The effect of castration on the penis in the guinea-pig is dependent upon the age of the animal at the time of castration. In the rabbit the retrogressive changes are independent of the age of the animal at the time of castration.—G. E. B.

The rôle of the interstitial gland of the TESTICLE. Response to Gley and Pézard (*A propos du rôle de la glande interstitielle du testicule. Response à MM. Gley et Pézard*). Bouin (P.) & Ancel (P.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 758-760.

Transplantation of TESTES. Brandt & Lieschied, *Ztschr. f. urol. Chir. (Berl.)*, 1923, 12, 460-467.

Brandt and Lieschied report 4 cases in which a testis was transplanted. No influence was apparent in 2 of the young men and the man, aged 52, but the fourth man, aged 29, was improved, but only transiently. Experiments on dogs confirmed degeneration of the testis into a cicatricial tissue.—*J. Am. M. Ass.*, 80, 1820.

OVARIAN extracts. Bru (C.), *Bull. méd. (Par.)*, 1923, 37, 430; cit., *J. Am. M. Ass. (Chicago)*, 1923, 80, 1814.

Influence of loss of vision on the function of the TESTES and on the external sex characters (*Der Einfluss der Sehkraft auf die Funktion des Hodens und auf die äusseren Geschlechtscharaktere*). Ceni (C.), *Arch. f. Entwicklungsmechn. d. Organ (Berl.)*, 1922, 51, 504-508.

Brain lesions in adult male chickens produce transitory changes in the testes and external sex characteristics. This is most marked

when the operation is done in the autumn and winter. After about 3 months of blindness the tubules of the testes have greatly atrophied while the interstitial cells have increased. Simultaneous with these changes are marked somatic changes in the feathers, comb, etc., and the animal stops crowing. Then there is a return towards normal. The loss of sexual characters during hyperplasia of the interstitial cells is cited as evidence against the assignment of a specific function to the interstitial cells.—A. T. R.

(GONADS) On the secondary sex characters in amphibia (*Sur les caractères sexuels annexes chez les amphibiens*). Champy (C.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 55-57.—T. C. B.

(GONADS) Sexual characters in fishes [*Observations sur les caractères sexuels chez les poissons (avec démonstration)*]. Champy (C.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 414-417.

The author thinks that the interstitial tissue plays no part in the development of sex characters in fish.—T. C. B.

(GONADS) Demonstration. Champy (C.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 852.

(GONADS) Fluctuating appearance of secondary male characters in female Tritons. (*Apparition fluctuante de caractères sexuels mâles chez Triton alpestris femelle*). Champy (C.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175, 1443-1444.

In certain female tritons, after egg-laying, male characters appear for a week or two, the animal then regaining a normal appearance. The phenomenon is correlated with total absence of oocytes of large size, indicating an inhibiting influence of the ovary on certain male characters.—A. T. C.

(GONADS) OVARIAN therapy. Clark (J. G.), *Progr. Med. (Phila.)*, 1921, 2, 229-230 (June).

A brief résumé of a paper by Graves on this subject (N. York M. J., 1920, 112, 697), presenting this author's views on the results of ovarian therapy. Ovarian extracts are advocated for the treatment of hot flushes, menstrual irregularities and functional amenorrhea. In dysmenorrhea this plan of treatment is unreliable. For menorrhagia and metrorrhagia it is not indicated.—E. N.

(GONADS) OVARIAN transplantation. Clark (J. G.), *Progr. Med. (Phila.)*, 1921, 2, 228-229 (June).

A brief description of Blair Bell's technique of transplantation. In the human being all grafts must be autoplasmic. After removal of the ovaries, the ovarian tissue for grafting is dropped into the bottom of the pelvis to be kept warm and moist until required for grafting. It is criss-crossed with a knife into adherent fragments after removal of the albuginea. The graft may be placed in the

rectus muscle. Bell strongly advocates grafting in suitable cases, but looks upon it as a measure of necessity, not comparable to preservation of the natural functions of the ovary.—E. N.

(GONADS) The interstitial cells of the TESTICLE and the secondary sex characteristics in the fish (*Glande interstitielle du testicule et caractères sexuels secondaires chez les poissons*). Courrier (R.), *Compt. rend. Acad. d. sc. (Par.)*, 1921, 172, 1316-1317.

Correction of *Endocrin.*, 1922, 6, 877.

(GONADS) The genital cycle of the female of certain hibernating mammals (*Le cycle genital de la femelle chez certain mammifères hibernants*). Courrier (R.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1365-1367.

A study of the oestrus cycle in the bat, which has but one a year. During 7 months the bat shows the following phenomena: rut, secretion of the uterus and oviduct, hyperplasia and keratinization of the vaginal epithelium.—T. C. B.

(GONADS) The glandular cycle of the epithelium of the oviduct in the dog (*Le cycle glandulaire de l'épithélium de l'oviducte chez la chienne*). Courrier (R.) & Gerlinger (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1363-1365.

The tubal epithelium in the dog possesses a glandular cycle of remarkable clearness which is in chronological relation with the ovarian processes.—T. C. B.

Delayed symptoms of OVARIECTOMY and the physiologic menopause (*Accidents tardifs de la castration ovarienne et ménopause physiologique*). Daléas (P.), *Thèse de Toulouse*, 1922; abstr., *Rev. franç. de gynéc. et d'obst. (Par.)*, 1923, 18, 64 (Jan.).

The author has reference particularly to the delayed symptoms which appear at the normal time of the menopause in cases in which castration has been previously performed. The disorders are chiefly nervous and are due to a general endocrine decay occurring at that time.—E. N.

(GONADS) Relations of endocrine glands with genital organs (*Les relations des glandes endocrines avec les organes génitaux*). Daniel (C.), *Rev. franç. de gynéc. et d'obst. (Par.)*, 1923, 18, 99-100 (Feb.).

Interstitial cells in the TESTIS of the Annelids, *Stilaria* and *Lumbricus* (*Les cellules interstitielles dans le testicule d'Annélides, Stilaria et Lumbricus*). Dehorne (A.), *Compt. rend. Acad. d. sc. (Par.)*, 1923, 176, 1674-1676.

(GONADS) Case of eunuchoidism. A pluriglandular syndrome with typical "lean geroderma genito-distrofico" (*Un caso de eunucoidismo. Síndrome pluriglandular, con hipogenitalismo congénito pre-*

dominante, realizando el tipo geroaderma génitodistrófico magro de Rummo y Ferranini). Echevarne (C. L.), *Semana méd.* (Buenos Aires), 1923, 30, 219-222.

Numerous symptoms of hereditary syphilis were found.

—B. A. H.

OVARIAN pathogenesis of chlorosis (*Pathogénie ovarienne de la chlorose*). Etienne (G.), *Rev. méd. de l'est* (Nancy), 1922, 50, No. 10 (May 15); *abst., Presse méd.* (Par.), 1922, 30, 936.

Since 1896 Spillmann and Etienne have considered chlorosis as due to vitiation of ovarian function. They consider it, on one hand, as a toxic disturbance caused by amenorrhea and the non-elimination of the toxic products of the feminine organism, and, on the other hand, as a profound disturbance of general metabolism, of nutrition of the tissues and of the condition of the blood,—caused by insufficient ovarian incretion. That this conception is correct has been demonstrated, Etienne states, by the effect of opotherapy on the number of red cells, on urinary metabolism and on health in general. He believes that the corpus luteum is the incretory gland of the ovary. Histologically, therefore, the ovary can be considered as a gland of internal secretion after the formation of the first corpus luteum. If the ovary does not function at the physiological moment chlorosis appears. The author believes it probable that before the ovary has begun to function its activity is carried on by a more precociously developed organ, perhaps the thymus. If this gland disappears too early or if the ovary develops its internal secretions too late chlorosis is seen. Thus, all circumstances capable of interrupting the normal development of the ovaries become etiologic factors in chlorosis. Ovarian opotherapy is advocated for chlorosis, with the addition of iron which the author thinks is fully effective only when taken along with the opotherapeutic treatment.—R. G. H.

(**GONADS**) A case of ectopic **TESTICLE** in the bat [*Note sur un cas d'ectopie testiculaire chez la chauve-souris (Vesperugo pipistrellus)*]. Faure (C. L.), *Compt. rend. Soc. de biol.* (Par.), 1922, 87, 1147-1148.

Histological.—T. C. B.

(**GONADS**) Concerning a free-martin. Firth (R.), *Vet. J.* (Lond.), 1921, 77, 340-342.

The influence of the GONAD hormones on the seminal vesicles. Fisher (N. F.), *Am. J. Physiol.* (Balt.), 1923, 64, 244-251.

The seminal vesicles in rats and guinea pigs are not reservoirs for spermatozoa or prostate secretion. The cells of the mucosa indicate secretory activity and transplantation to other parts of the body does not interfere with this secretory activity. Early bilateral castration inhibits the growth of the vesicles; later castration causes

atrophy without total inhibition of secretion. The seminal vesicles are not affected by the presence of ovarian grafts in normal males.

—T. C. B.

X-ray stimulation in hypofunction of the OVARY (*Über Reizbestrahlung bei Hypofunktion der Eierstöcke*). Flatau (W. S.), *Zentralbl. f. Gynäk.* (Leipz.), 1922, 46, 1602-1606.

In infantilism, medical treatment of amenorrhea or dysmenorrhea never gives a good result. Special symptoms are seen in these subjects: swollen face, adiposity, symptoms as in the menopause, psychical irritability, etc. Van der Velde, Momm and others have advised the use of x-rays in so-called stimulating doses. The author tried this treatment in 38 subjects and in 26, regular menstruation was obtained in 3-6 weeks. This treatment is indicated only in cases in which the abnormal menstruation is caused by hypofunction of the ovary; x-ray therapy should not be used in adiposogenitalis.—J. K.

(GONADS) Organotherapy of menstrual disorders (*Opothérapie des troubles menstruels, opothérapie lutéique dissociée*). Fouliot (L.), *Paris méd.*, 1922, 12, 434-437 (November 11); cit., *J. Am. M. Ass.* (Chicago), 1922, 79, 2197.

(GONADS) The endocrine function of the sexual organs and its practical importance (*Über die innere Sekretion der Keimdrüsen und ihre praktische Nutzenanwendung*). Fraenkel (L.), *Ztschr. f. ärztl. Fortbild.* (Jena), 1922, 19, 585-590.

The author believes that the function and nutrition of the entire sexual apparatus depends upon the incretion of the ovary or testicle. Another function of the ovary which is dependent upon its internal secretion is the preparation of the mucous membrane of the uterus for the insertion of the ovum. This last function is carried out especially by the corpus luteum. It is remarkable that insufficiency of one or more endocrine organs never causes hyperfunction of the ovary, but that, on the other hand, hypofunction of the ovary immediately causes hyperfunction of the whole endocrine system. Fraenkel feels that in spite of the extensive literature on the subject, little is actually known concerning the incretory glands and their interrelations.—J. K.

Functional significance of the interstitial cells of the TESTIS (*Zur Frage der funktionellen Bedeutung der Hodenzwischenzellen*). Frankenberger (Z.), *Anat. Anz.* (Jena), 1922, 55, 545-550.

A brief description of the finer structure of the testis of a lizard (*Lacerta vivipare* Jacz.).—A. T. R.

The action of heat ray on TESTICLES. Fukui (N.), *Jap. Med. World* (Tokyo), 1923, 3, 26-28.

Heat applied to the scrotum of the rabbit always caused typical regressive changes in the generative cells of the testicles. Such testicle the author designates as "heat testicle." In the production of heat testicle there is a definite relation between temperature and time, the highest temperature used being 48° C. and the lowest, 40° C., i.e. body temperature. At the higher temperatures the changes occur rapidly and below 44° C. the rate of change is greatly lengthened. When the exposure is all given at one sitting the changes occur much more rapidly than when they are given on succeeding days. Midsummer sunlight caused a similar effect within 3 hours. This was only partly avoided by the use of a cotton covering. These changes are important in Japan because of the type of clothing and the custom of taking very hot baths. The author raises the question whether a thermolabile spermatogenous protein is the reason for the descent of the testicle, what effects modern clothes and hygiene have upon this and what effect the "heat testicle" has on other endocrine glands.—R. G. B.

(GONADS) Conservatism in the treatment of "essential uterine hemorrhage." Geist (S. H.), Surg. Gynec. & Obst. (Chicago), 1923, 36, 383-384 (March).

Report of 4 cases of atypical bleeding, in which the uterus was grossly normal, and in which both ovaries were found to be diseased (cystic). Good results followed resection of both ovaries.—E. N.

(GONADS) Syndromes associated with OVARIAN disorders (Les syndromes dûs aux troubles ovariens). Gheorghiu (E.), Rev. franç. de Gynéc. et d'obst. (Par.), 1923, 18, 98.

No new facts.—E. N.

OVARIAN secretion in parabiosis. Goto (N.), Tokyo Igakkwai Zasshi, 1922, 36, No. 9; abst., Jap. Med. World (Tokyo), 1923, 3, 12; see also, Arch. f. exper. Path. u. Pharmacol. (Leipz.), 1922, 94, 124-128.

Matsuyama observed an interesting change occurring in the ovary of a parabiosis of a castrated and a normal animal, and also after injection of the blood from a castrated rat into a normal rat. This substance may be present to some extent in the normal animal. The author has not isolated the substance causing this change.

—R. G. B.

An attempt to obtain rejuvenation by transplantation of a TESTICLE taken from a corpse (Ein Verjüngungsversuch mit Transplantation von Hoden, die einer Leiche entnommen wurde). Gregory (A.), Zentralbl. f. Chir. (Leipz.), 1922, 49, 1326-1327.

A man of 68 complained of being easily tired, of difficult breathing and loss of sexual desire. The author transplanted into this subject a testicle from the corpse of a man who had died with

tuberculosis—these patients generally have increased sexual desire. The testicle was divided into 2 parts which were implanted on both sides between the obliquus muscles, external and internal, and the transverse abdominal muscle. The patient was cured; he lost his feeling of exhaustion and regained the sexual desires he had had when 40. The author states that although the results seem very good it is not known how long the improvement will last.—J. K.

(GONADS) Application of Steinach's method in zoötechnics. Its value in rejuvenation of reproduction (Aplicación del metodo de Steinach en zootecnia. El rejuvenecimiento de reproductores). Grosovich (J. M.), *Rev. zootéc.*, 1921, 8, 183-185.

Steinach's method of rejuvenation might be tried by cattle breeders to bring about reproductions among cattle otherwise too old.—B. A. H.

(GONADS) Psychology in castrates (Testicule et psychologie des castrats). Grynfeldt, *Bull. Acad. d. sc. de Montpellier*, (1921) 1922, 38-40.

(GONADS) Sex stimulation and rejuvenation (Das Problem der Geschlechtsumstimmung und die sogenannte Verjüngung). Harms (W.), *Naturwissenschaften (Berl.)*, 1921, 9, 184-189.

(GONADS) Present status of the puberty gland. Hart (C.), *Med. Klin. (Berl.)*, 1922, 18, 803 (June 18); cit., *J. Am. M. Ass. (Chicago)*, 1922, 79, 2043.

(GONADS) Relation of the OVARY to the gravid uterus in the aplacental opossum. Hartman (C.), *Am. J. Physiol. (Balt.)*, 1923, 63, 423-424 (Proc.).—T. C. B.

(GONADS) Solid carcinoma of the OVARY. Hoon (M. R.), *Ann. Surg. (Phila.)*, 1922, 76, 768-776 (December); cit., *J. Am. M. Ass. (Chicago)*, 1923, 80, 354.

(GONADS) Clinical and experimental studies on the transplantation of the TESTICLES. Ishiyama (F.), *Iji Shimbun (Tokyo)*, 1922, No. 1102 (September).

The author's trial transplantation of the isogenic testicle in a human case proved negative. All cases of the testicle transplantation in the rabbit resulted in necrosis. Of all the cellular elements of the testicle the one that had the most remarkable resistance was the spermatozoa, which lived long after the seminal tubules and the interstitium had necrosed. Both Sertoli's cells and the seminal cells died out very soon. Leydig's cells also died out as soon as the interstitium necrosed. However, rapid necrosis occurred if a piece, the whole or the epididymis of the testicle has been transplanted.

—*Jap. Med. World*, 2, 348.

Pathological changes in the GONADS in constitutional diseases, particularly marasmus (Patologisch-anatomische Veränderungen der Keimdrüsen bei Konstitutionskrankheiten, insbesondere bei der Pädatrophy). Jaffe (R.), Verhandl. d. deutsch. path. Gesellsch. (Jena), 1921, 18, 204.

See Endocrin., 6, 567.

Influence of castration on the structure of the PANCREAS and THYROID (Über den Einfluss der Kastration auf den Bau der Bauchspeicheldrüse und der Glandula thyreoides). Kanewskaja (E. I.), Verhandl. d. Russ. Path. Ges. (Petrog.), 1920, 11; abst., Ber. ü. d. ges. Physiol. (Berl.), 1922, 14, 176.

In castrated animals the author noted hypertrophy of the islands of Langerhans and of the thyroid gland. The experiments will be reported in detail in other articles to follow.—R. G. H.

(GONADS) Theory concerning the interstitial cells (Theoretisches zur Zwischenzellenfrage). Kolmer (W.), Klin. Wchnschr. (Berl.), 1922, 1, 2022.

The author does not consider the interstitial cells as endocrine organs, nor does he believe that their function is trophic. He believes that the male cells protect the male organism against substances of female origin and vice versa. In bats the sperm remains in the uterus for 6 months, and, therefore, these animals have enormous numbers of interstitial cells.—J. K.

Action of alcohol on the interstitial cells of the TESTICLE (Action de l'alcool sur la glande interstitielle du testicule). Kostitch (A.), Internat. Ztschr. gegen. d. Alkoholismus, 1922, 30, 134-138; abst., Ber. ü. d. ges. Physiol. (Berl.), 1923, 16, 389.

The interstitial cells remain normal during the first changes in the epithelium, but as the degeneration of the epithelium increases the interstitial cells continue to increase in number, finally appearing between the tubules, which were before in apposition; pushing them ahead and crowding them apart until they are almost obliterated. Alcohol poisoning leads to hypertrophy of the interstitial glands. In a condition of long standing pigment atrophy of the interstitial cells sets in, leaving finally only heaps of pigment granules. The general condition of the animal is not affected thereby, and libido may remain rather strong. The author assumes that the hypertrophy is a direct result of alcohol, which also stimulates the interstitial cells in their defensive proliferation, this being favored by the shrinkage of the tubules. This reaction has damaging effects on the seminal elements.—R. G. H.

(GONADS) Tubercle sclerosis of the brain and hydrocephalus in relation to early puberty [La sclérose tubéreuse du cerveau (maladie de Bourneville) et l'hydrocéphalie dans leurs rapports avec la

puberté précoce]. Krabbe (K. H.), *Encéphale* (Par.), 1922, 17, Nos. 5, 7, 8; abst., *Presse méd.* (Par.), 1923, 31, Analyses 16 (April 7).

GONADS in 30 newborn goats. One case of true unilateral hermaphroditism (*Eine Untersuchung der Geschlechtsdrüsen von dreißig neugeborenen Ziegen. Ein Fall von wahrem unilateralen Hermaphroditismus*). Krediet (G.), *Anat. Anz.* (Jena), 1922, 55, 502-510.

Description of an ovariostestis. One seminiferous tubule even contained a primary ovarian follicle.—A. T. B.

TESTICULAR transplantation in human beings (*Weitere Erfahrungen über Hodentransplantation beim Menschen*). Kreuter (E.), *Deutsche Ztschr. f. Chir.* (Leipz.), 1922, 172, 102-116; abst., *Ber. ü. d. ges. Physiol.* (Berl.), 1923, 17, 64.

The results of experiments and observations made by the author were entirely negative. In 2 cases at the end of 2 years the transplanted organ had entirely disappeared. In another case the implantation of a heterosexual active testicle into a homosexual subject, castrated on one side, was ineffective, and the implantation of a homosexual testicle into a subject castrated on both sides, originally heterosexual, led to no success.—R. G. H.

(GONADS) MENSTRUATION—An inquiry into its etiology. Kross (I.), *Am. J. Obst. & Gynec.* (St. Louis), 1923, 5, 285-287 (March).

The author concludes, from the evidence of two inconclusive clinical cases, that the corpus luteum is not the causative factor in menstruation, and that the mature graafian follicle is —E. N.

Interstitial-like element in an accessory **TESTICLE** (*Über zwischenzellen-ähnliche Elemente im Nebenhoden*). Kyrle (J.), *Beitr. z. path. Anat. u. z. allg. Path.* (Jena), 1922, 70, 520-524; abst., *Ber. ü. d. ges. Physiol.* (Berl.), 1923, 17, 375.

Occurrence of the interstitial cells of the **TESTIS** in the embryonic and postnatal life history of the guinea pig. Kudo (T.), *Folia anat. Jap.*, 1922, 1, 125-148; abst., *Ber. u. d. ges. Physiol.* (Berl.), 1923, 17, 22.

(GONADS) Infantile gigantism (*Infantiler Riesenwuchs*). Kun-dratitz, *Wien. med. Wchnschr.*, 1921, 71, 1814.

(GONADS) Androgenoids and gynandroids (*Les androgynes et les gynandres*). Laignel-Lévestine, *Progrès. méd.* (Par.), 1920, 35, 399-403.

(GONADS) A case of gynandrism similar to hypospadias (*Sur un cas de gynandroïde simulant un hypospadias*). Lepoutre (C.), *J. d'urolog. méd. et chir.* (Par.), 1921, 11, 229-231.

The definite result of transplantation of GONADS in man (*Die Dauer-
verfolge der Hodentransplantation beim Menschen*). Lichtenstern,
Klin. Wchnschr. (Berl.), 1922, 1, 2598.

See Endocrin., 5, 807.

Hypertrophy of the INTERSTITIAL CELLS. The conditions govern-
ing its occurrence (*Ueber die Hypertrophie der Zwischenzellen.
Ihr Vorkommen und ihre Bedingungen*). Lipschütz (A.) & Wag-
ner (K.), Arch. f. d. ges. Physiol. (Berl.), 1922, 197, 348-361.

Experiments on guinea pigs lead to the conclusion that hyper-
trophy of the interstitial cells, like that of the generative tissue,
cannot be regarded as a compensatory reaction of the testes in their
internal secretory function. In certain conditions the hypertrophy is
great, and it is easily possible to distinguish whether an absolute
increase of tissue mass is present. The local conditions governing
the hypertrophy appear to be either retrograde development of the
seminiferous tubules or good circulation, the latter probably acting
directly through its acceleration of spermatogenesis. A general
favorable condition of hypertrophy would seem to be the reduction
of the testicular mass (partial castration) by which are accelerated
spermatogenesis, retrograde development of the tubules, and com-
mencement of hypertrophy of the interstitial cells.—A. T. C.

The effect of extirpation of the uterus on the life and function of the
CORPUS LUTEUM in the guinea-pig. Loeb (L.), Proc. Soc. Exper.
Biol. & Med. (N. Y.), 1923, 20, 441-443.

Extirpation of the uterus prolongs the life of the corpora lutea
up to 60 days and even longer. These corpora lutea function nor-
mally in preventing ovulation and producing proliferation in the
mammary gland. Hysterectomy does not prevent ovulation. If a
small part of the uterus is left in place the sexual cycle remains
normal.—J. C. D.

GONADS The mechanism of the sexual cycle and the specificity of
growth substances. Loeb (L.), Proc. Soc. Exper. Biol. & Med.
(N. Y.), 1923, 20, 443-445.

The author considers the cycle as consisting of 3 phases. In
the first the changes in the animal are brought about by the matur-
ing follicle. In the second phase there is a transition from the
control by the follicle to the third stage, that governed by substances
elaborated in the lutein cells. Evidence for this view is given,
derived from observations on rats, mice, and guinea-pigs.—J. C. D.

Types of mammalian OVARY. Loeb (L.), Proc. Soc. Exper. Biol. &
Med. (N. Y.), 1923, 20, 446-448.

Descriptions of the 3 types are given with a suggestion as to
why the theca cells differ.—J. C. D.

(GONADS). Effect of PROSTATECTOMY on integration of muscular movements of the rat. Macht (D. I.) & Ulrich (J. L.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 186-187.

In rats that had been trained to walk a tight rope, a removal of the prostate did not impair this ability. When the prostate was removed previous to training, however, rope walking was mastered only with difficulty and never as perfectly as in the controls. Feeding prostate improved this ability.—J. C. D.

(GONADS) 'Bisexual stages (Intersexuelle Zwischenstufen). Magnus-Hirschfeld, Deutsche med. Wchnschr. (Berl.), 1923, 49, 500.

Recent biological and psychological studies confirm the theory given 24 years ago by the author that every man has predominant male with some female characteristics, and vice versa.—J. K.

Menopause age in Finland (Über das Alter der Menopause in Finnland. Eine statistische Studie). Malmio (H. R.), Acta soc. med. fennic. "Duodecim," 1921, 3, 1-16; abst., Ber. ü. d. ges. Physiol. (Berl.), 1922, 12, 133.

After a criticism of the modern statistics on the appearance of menopause in Finland, the author gives 220 case histories of patients from an institution for the poor. The subjects were from 55 to 80 years old, had never undergone any chronic illness and could remember positively the occurrence of the menopause. The mean value for the menopause age was found to be 48.66 ± 0.36 years. For women of Finland (160 cases) the mean value was 48.62 ± 0.42 years; of Swedish nationality (60 cases) 48.58 ± 0.69 years; thus the difference is rather insignificant. Menopause appeared somewhat late in women with one or two children, but in women having more children occurred a little earlier. The age at which menopause occurred seemed to be independent of the menarche age. Only the very early and very late variants of the series conformed to some law. Following this another investigation was made on subjects from the gynecological clinic of Helsingfors. The average found there was 48.53 ± 0.18 years, this average being in accordance with that of the first group. Various mistakes are likely to be made, however, in summarizing; if the dubious data are excluded from the statistics another average, 49.50 ± 0.24 years, is found. Since an investigation of the menopause age in the different gynecological disturbances, with the exception of malignant tumors, shows delayed menopause, it is doubtful whether the material from a gynecological clinic is suitable for the purpose of establishing an average national menopause age. The average menarche age in Finland is 16.089 ± 0.050 years and the age of sexual maturity of women in Finland is 32.5 years.—R. G. H.

(GONADS) The hypogenital hand (*La main hypogenitale*). Marañón (G.), *Rev. de méd. (Par.)*, 1922, 39, Nos. 10, 11; abst., *Presse méd. (Par.)*, 1923, 31, 187.

See *Endocrin.*, 7, 481.

(GONADS) A case of masculine spurious hermaphroditism (*Un caso di ermafroditismo spurio maschile*). Mariani (A.), *Pensiero med. (Milano)*, 1921, 11, 581-585.

In a bilateral hernia in a "woman" was seen two small, incompletely developed testes. External genitalia were normal except for the lack of the labia majora. The vagina was only 4 cm. in length. No uterus nor ovary was present. The secondary sexual characters were feminine. The author concludes that the sexual characters are related not only to the gonads, but also to some other gland.—P. N.

The interstitial cells of the OVARY of the new-born (*Die interstitielle Eierstockdrüse beim Neugeborenen*). Matsuno (J.), *Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.)*, 1923, 85, 523-539.

The ovaries of some 25 new born or late fetal stage infants were studied histologically. The wide variability in apparent follicular development precludes adequate generalizations. The histological picture is not sufficiently convincing to permit the conclusion of an internal secretory function at this early age.—F. S. H.

The lipoids in the human OVARY (*Ueber die Lipoide in menschlichen Ovarium*). von Mikulicz-Radecki, *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1192-1193; see also, *Klin. Wchnschr. (Berl.)*, 1922, 1, 1389-1390.

During the development from corpus luteum of menstruation to corpus luteum gravidarum and during the formation of the corpus atreticum the quantity and quality of the lipoids undergo important changes. As long as the cells function, lipoids containing nitrogen and phosphorus and optically active substances, such as mixtures of cholesterol and cephalin, are present. The first symptom of degeneration is the occurrence of neutral fats. These substances gradually increase and at last only neutral fats, fatty acids and soaps are found. The complicated lipoids, phosphatids, cerebrosids, cholesterol, the author considers as the hormones produced by the endocrine function of the lutein cells. They are identical with the ovarian lipoids which many investigators have used to demonstrate the influence of the ovary on the body. On the contrary, the lipoids in the interstitial tissue are products of degeneration. The theca lutein cells do not produce active lipoids.—J. K.

The effects of GONAECTOMY in the guinea pig, on growth, bone lengths, and weight of organs of internal secretion. Moore (C. R.), *Biol. Bull. (Woods Hole)*, 1922, 43, 285-312.

This paper gives a really critical study of the variations produced in total body weight and in the relative weights of certain organs by gonadectomy. A series of guinea pigs consisting of 12 normal and 11 castrated males and 12 normal and 11 spayed females was used. The operations were performed between the fifteenth and the thirtieth days of the animal's life and the observations covered a period of a year. The weights of the gonadectomized animals of this series were less than those of their normal controls, but the writer points out that there is so much individual variation that body weight is not a reliable criterion of sex gland conditions. The experiments indicate that gonadectomy in both sexes causes a slight reduction in the weight of the hypophysis, adrenals and spleen, and a slight increase in the size of the thyroid. Spaying seems to cause more increase in the length of the leg bones than does castration. The changes produced by the operation are not very marked and the author advises making more experiments of the same sort before attempting to formulate any general principles.—M. M. H.

Case of ectopia TESTES. Morson (A. C.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 43-44.

(GONADS) Condition of sex organs in dementia praecox. Mott (F. W.), Encéphale (Par.), 1923, 18, 73-85.

Mott has been studying since 1910 the findings in the reproductive organs in mental disorders, particularly dementia praecox. In 34 cases of general paralysis, spermatozoa were found nearly always present, while in 37 cases of dementia praecox, spermatozoa were found in only 2 cases out of 3. The reproductive organs are closely connected with other endocrine glands and his research on suprarenal glands has demonstrated that the medulla of these glands in dementia praecox shows vast deficiency in the genetic formative impulse.—J. Am. M. Ass., 80, 1814.

Internal secretion of the human OVARY (La glande à sécrétion interne de l'ovaire humain). Moulonguet-Dolérès (P.), Gynéc. (Par.), 1923, 22, 129-162.

An anatomical and physio-pathological study of much detailed description. Microscopic study led to the conclusion that the principal dépôt of the lipoids in the human ovary is not the corpus luteum but in a type of structure designated by the author as the "ovarian stroma." These lipoid formations are believed to be most important from the point of view of the endocrine physiology of the ovary. There is, however, a wide variability in the lipoid content of human ovaries. The variations are described in detail in the text. One particular type which is considered of physio-pathological significance is characterized by the coexistence of numerous masses of spongiocytic cells with pycnotic nuclei accompanied by many external cells of the corpus luteum. These cells are crowded with

labile lipoids. From a correlation of histological and clinical observations it is concluded that there is no direct and constant relation between the richness of the ovary in lipoids and uterine metrorrhagias, but that exaggerated mucous hyperplasia of the endometrium is often associated with hyperplasia of the ovary, as is fibromyoma.—F. S. H.

(GONADS) Sexual constitution and surgery (*Sexualkonstitution und Chirurgie*). Mühsam (R.), *Deutsche med. Wchnschr. (Berl.)*, 1923, 49, 500.

Sexual symptoms may be influenced by ablation of the testicles. The transplantation of a testicle may have a very marked influence which, however, is usually temporary. It is not known whether Steinach operations are effective. The author states that it may be possible to change sexual abnormalities by operation on the adrenals, pineal, hypophysis and thyroid. Up to this time practical surgery has not made investigations along this line.—J. K.

(GONADS) End results of TESTICLE transplantation (*Endergebnisse der Hodenüberpflanzung*). Mühsame (R.), *Deutsche med. Wchnschr. (Berl.)*, 1922, 48, 1341-1343.

Report of 6 transplantations in 5 patients. On April 6, 1918, a testicle was implanted in a castrated man. In November, 1918, there was return of libido. In March, 1919, he married and had normal sexual intercourse. A bisexual man of 20 was operated upon April 9, 1919. He soon had "heterosexual inclinations" and sexual intercourse. He married and became the father of a child. Testicle transplants were made twice in a homosexual man. After both operations there was a short heterosexual period, but there was no lasting affect. In a homosexual man one testicle was removed and another implanted. At first the operation did not seem to be a success, but 4 months afterwards the man was normal. In a eunuchoid 30 years of age the only effect of the transplantation was a number of erections for a short period after the operation.—J. K.

(GONADS) The relation between the internal secretion of the genital glands and skin diseases. Nakagawa (K.), *Hifuka Hitsunyokika Zasshi*, 1922, 22, No. 9 (Sept.); cit., *Jap. Med. World (Tokyo)*, 1923, 3, 55.

The transplantation of human TESTICLES. Nakada (M.), *Tokyo Iji-Shinshi*, 1922, No. 2301 (Oct.); abst., *Jap. Med. World (Tokyo)*, 1923, 3, 31.

In a case of tuberculous epididymitis a testicle was transplanted. For a few months the effect was beneficial, then relapse occurred.

—R. G. H.

GONADS in the adult *Rana fusca* (Demonstratie van een volwassen testis van *Rana fusca*). van Oordt (G. J.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, 66 (II), 2223-2224.

The sex glands of *Rana fusca* first develop along female lines; therefore, it is not a rare occurrence to find ova in the testes. The author observed such a testicle.—J. K.

(GONADS) The summer involution of secondary sex characters of the plumage of the drake, and the parallel modification of its **TESTICLES** (Sur l'involution estivale des caractères sexuels secondaires du plumage chez le canard mâle et sur les modifications parallèles du testicules chez le même animal). Parhon (C. I.) & Parhon (Constance), Compt. rend. Soc. de biol. (Par.), 1922, 87, 1227-1229.

Parallel with changes in color that come on about the first of August the testicles diminish in volume, spermatogenesis becomes less abundant, and there are changes in the cells. The interstitial gland is more developed than during the spring.—T. C. B.

(GONADS) A Steinach preparation for rejuvenation (Ueber Rejuven, ein Steinach-Präparat). Pariser (C.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1384-1385.

The author reports without sustaining evidence successful use of a tablet containing the chemical components of the testicle.—J. K.

(GONADS) The castration of decapoda Crustaceans through Epicaridae parasites (Sur la castration des Crustacés décapodes parasités par des Epicarides). Perez, Compt. rend. Acad. d. sc. (Par.), 1923, 176, 1934-1936.

These parasites exercise an indirect, harmful influence on the genital activity of their hosts. Where the parasite is installed before the development of sex characters in the host, as in Leander, Palaeomon, Pandalus, etc., these characters can be profoundly modified, so that, for example, the abdominal appendices of the male approach the female type. Crabs are less affected, the incomplete castration being manifest in a varying degree of atrophy of the genital gland.

—A. T. C.

GONADS and the nervous system (Keimdrüsen und Nervensystem). Peritz, Deutsche med. Wchnschr. (Berl.), 1923, 49, 500.

A short note.—J. K.

Conservation and transplantation into the uterus of an **OVARIAN** fragment after salpingectomy. Later pregnancy in one case (Conservation et transposition dans l'utérus d'un fragment d'ovaire après salpingectomie pour suppuration. Grossesse consécutive dans un cas). Petit (R.), Gynéc. (Par.), 1923, 22, 43-44; see also, Rev. franç. de gynéc. et d'obst. (Par.), 1923, 18, 58-59 (Jan.).

Report of 2 cases in which after salpingectomy a portion of an ovary was implanted into the uterus at the site of the emergence of the fallopian tube. The first patient, a woman of 32, menstruated regularly after the operation and became pregnant 2 years later. The second patient, a girl of 18, resumed menstruation 5 months after operation.—F. S. H.

Tumors of the interstitial gland of the TESTIS of the horse (*Sur les tumeurs de la glande interstitielle du testicule du cheval*). Peyron (A.), *Compt. rend. Acad. d. sc. (Par.)*, 1921, 172, 625-627.

Report of the general results of a histological study of 25 cases, unrelated to the functional conditions of the subjects. The histological condition is similar to that in homologous tumors in human testes.—A. T. C.

(GONADS) The "all-or-none" law and the gynandromorphism of birds (*La loi "tout ou rien" et le gynandromorphisme chez les oiseaux*). Pézard (A.), *J. de. Physiol. et de path. gén. (Par.)*, 1922, 20, 495-508.

The "all-or-none" law prevails—so far as the incretory genital tissue is concerned—above a certain minimum or threshold, below which the morphogenic effect is zero; the amount is sufficient to cause secondary sexual characters to appear and undergo complete development. The threshold is not the same for all these characters, however, and there is consequently a differential threshold for the different aspects of the secondary sex characteristics.—W. B. C.

(GONADS) The theory of the "threshold difference" and progressive masculinization in certain female birds (*Notion de "seuil différentiel" et masculinisation progressive de certaines femelles d'oiseaux*). Pézard (A.), *Compt. rend. Acad. de sc. (Par.)*, 1922, 175, 236-238; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1922, 15, 480.

(GONADS) A "differential threshold" and humoral explanation of the gynandromorphism of bipartite birds (*Notion de "seuil différentiel" et explication humorale du gynandromorphisme des oiseaux bipartis*). Pézard (A.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 174, 1573-1576.

A theoretical discussion with no new evidence.—A. T. C.

Sex heredity in the Gallinae. Interpretation based on the existence of the neuter form and on the properties of the OVARIAN hormone (*L'hérédité sex-linked chez les Gallinacés. Interpretation fondée sur l'existence de la forme neutre et sur les propriétés de l'hormone ovarienne*). Pézard (A.) & Caridroit (F.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175, 910-912; abst., *Ber. ü. d. ges. Physiol. (Berl.)*, 1923, 17, 312.

(GONADS) Gynandromorphism in fowls (*Les modalités du gynandromorphisme chez les gallinacés*). Pézard (A.) & Caridroit (F.), *Compt. rend. Acad. d. sc. (Par.)*, 1923, 177, 76-79.

A white leghorn developed female characters at puberty; some weeks later these were transformed to male characters. Autopsy revealed 2 reproductive glands, one occupying the normal position on the left side and consisting of an infantile ovary showing masculine development with an infantile oviduct, the other symmetrically on the right side being a testis with abundant interstitial tissue and without a duct.—A. T. C.

(GONADS) ADRENAL-TESTICULAR interpenetration in cocks incompletely castrated. Pézard (A.) & Caridroit (F.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175, 784-787.

Following incomplete castration can be observed invasion of accidental testicular transplants by adrenal medullary tissue, and the presence of seminiferous canals in the interior of the adrenal, which show signs of functional activity even after a year.—A. T. C.

(GONADS) Action of the TESTICULAR hormone on the relative value of allélomorphic factors in fowls (Dorset x Suffolk) [*L'action de l'hormone testiculaire sur la valence relative des facteurs allélomorphes chez les ovins (Dorset x Suffolk)*]. Pézard (A.) & Caridroit (F.), *Compt. rend. Acad. d. sc. (Par.)*, 1922, 175, 1099-1102.

Introduction of the neutral form and the testicular hormone into the genetic analysis of Dorset x Suffolk crosses leads to a clear interpretation of the facts.—A. T. C.

Torsion of the TESTICLE in a pseudohermaphrodite (*Sopra un caso di torsione del testicolo osservata in un pseudo-ermafrodito*). Pignatti (A.), *Riforma med. (Napoli)*, 1921, 37, 605-610.

Dermoid cyst of the OVARY containing THYROID. Cesarean section with ovariectomy (*Kyste dermoïde de l'ovaire à contenu thyroïdien. Césarienne suivie d'ovariotomie*). Plauchu & Gaudon, *Bull. Soc. d'obst. et de gynéc. (Par.)*, 1923, 12, 134-135.

(GONADS) Secondary sex characters in the male lizard (*Sur les caractères sexuels secondaires chez le lézard male*). Reiss (P.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 445-447.

(GONADS) Hermaphroditism in animals (*Zur Frage des Hermaphroditismus beim Wildin*). Reuter (M.), *Ztschr. Forst Jagdwesen*, 1922, 54, 107-110; cit., *Anat. Ber. (Jena)*, 1922, 1, 21.

(GONADS) Recent studies on the relation of metabolism to sex. Riddle (O.), *Anat. Record (Phila.)*, 1923, 24, 418.

The adrenals of pigeons undergo marked hypertrophy coincident with each ovulation period. Accompanying this there is a marked

rise in blood sugar. Ova produced under treatment with thyroid substance become markedly and consistently smaller. Thymus feeding has no effect.—W. J. A.

Transplantation of an OVARIAN fragment into the uterus (*Sur la transplantation dans l'utérus d'un fragment d'ovaire*). Robineau, Gynec. (Par.), 1923, 22, 44-45.

Following Petit's technic, 2 subjects responded with increased menstrual flow, but no pregnancies occurred. Unilateral ovariectomy, accompanied by partial section of the uterus and removal of the tubes did not stop menstruation in 27 out of 28 cases.—F. S. H.

Types of rabbit OVARY from the physiological point of view (*Les types d'ovaire de la lapine au point du vue physiologique*). Salazar (A. L.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 838-840.

(GONADS) Some sex problems (*Einige Geschlechtsprobleme*). Sand (K.), Wchnschr. ü. d. Fortschr. in Wissensch. u. Technik (Frankfurt), 1922, 26, No. 40.

See Endocrin., 7, 273-301.

(GONADS) Vasoligature (epididymectomy) employed ad mod. Steinach with a view to restitution in cases of senium and other states (impotency, depression). Sand (K.), Acta chir. Scand. (Stockholm), 1922, 55, 387-426.

(GONADS) Experimental hermaphroditism (*l'hermaphrodisme expérimental*). Sand (K.), J. de Physiol. et de path. gén. (Par.), 1922, 20, 473-487.

An account of the production of hermaphroditic characters, somatic and psycho-sexual, in a considerable percentage of guinea pigs in which both ovaries and testes were present. These characters appeared whether the operation was performed on the animals while infantile, or at the age of puberty, or at the age of maturity and reproduction. In the last case the effects were especially marked on the mammary glands and on the psycho-sexual features.—W. B. C.

(GONADS) Alternating hermaphroditism. Sand (K.), J. d'urol. (Par.), 1923, 15, 181-195; abst., J. Am. M. Ass. (Chicago), 1923, 80, 1882.

Conservative operation for myoma with reference to the OVARIAN origin of myomal bleeding (*Ueber Konservative Myomoperation mit besonderer Berücksichtigung des ovariellen Ursprunges der Myomblutungen*). Schmid (H. H.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.), 1923, 86, 36-74.

(GONADS) Transplantation of OVARIES. Schochet (S. S.), Surg. Gynec. & Obst. (Chicago), 1921, 32, 567.

A very brief record of two observations. The first pertains to

the eye of a pregnant rabbit in which is a transplanted ovary (a quadrant) showing no sign of ovulation. This concurs in part with the theory of L. Fraenkel. The second has to do with an ovum, artificially fertilized from a transplanted ovary and tube, an ectopic pregnancy.—E. N.

(GONADS) Substances which stimulate genital growth (Ueber Substanzen die das Genitale wirksam zum Wachstum anregen). Schroder (R.) & Goerbig (F.), *Ztschr. f. Geburtsh. u. Gynäk.* (Stuttg.), 1921, 83, 764-786.

An extensive series of experiments in which the action of placental and corpus luteum preparations on uterine growth was studied. Stimulation was produced both in the females and in the male subjects (utriculus masculinus). Other glandular products produced no marked effects, except that liver extract seemed to be efficacious.—F. S. H.

OVARIAN transplantation in deficient genital function (Die Ovarien transplantation bei herabgesetzter und fehlender Genital-funktion). Sippel (P.), *Arch. f. Gynäk.* (Berl.), 1923, 118, 445-489.

Detailed clinical protocols of the results of ovarian transplantation in various cases of genital insufficiency. It was found that auto-transplantation retarded the climacteric phenomena of castration in young women for some years. Homotransplantation is recommended in infantilism and hypo-ovarianism, in young castrates and selected cases of early climacteric or senility. Libido and orgasm are almost always renewed after autotransplantation; after homoplastic transplantation the results are variable. The function of the autoplant lasts from 1 to 3 years; that of the homoplant not more than a few months. The most difficult cases are those in which the whole reproductive system has begun to retrogress. A deficient thyroid function is usually also present.—F. S. H.

(GONADS) The oestrus cycle in the oviduct of the sow (Le cycle oestrien dans l'oviducte de la truie). Spack (A.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 450-452.

Experimental studies of two important factors underlying masculine sexual behavior: the nervous system and the INTERNAL SECRETION of the TESTIS. Stone (C. P.), *J. Exper. Psychol.*, 1923, 6, 85-106.

The author attempts to consolidate the literature concerning the nervous system and the internal secretion of the testis as concerned in masculine sexual behavior. After reviewing the literature it is concluded that the copulatory response of the male of higher vertebrates, considered from a neurological standpoint, is similar to those complex patterns of congenital behavior typified by the "scratch reflex" described by Sherrington. Although the brain and brain-

stem exert a regulatory influence over the copulatory response, there is no cortical center for its control. Erection and ejaculation are essentially a series of coordinated spinal reflexes involving the lumbosacral portion of the cord. The fundamental difference between the copulatory response and the "scratch reflex" is that the former depends upon a special gland for activation and regulation. That the internal secretion of the testes exerts its regulatory influence chiefly through the nervous system has been assumed but the mode and seat of action are unknown.—W. W. T.

(GONADS) Atrophy of the TESTES after extirpation of the abdominal sympathetic (Hodenatrophie nach Exstirpation des abdominalen Grenzstranges). Takahashi (N.), Arch. f. d. ges. Physiol. (Berl.), 1922, 196, 237-242.

Sympathetic extirpation produces no effects on kidneys, adrenals, ovaries, the hinder skeletal bones, nor the arteries. The testes atrophy (guinea-pigs), weighing distinctly less than the control after one-sided operations, and showing histologically reduction of sperm-epithelium without increase of the intertubular connective tissue and the characteristic interstitial cells.—A. T. C.

(GONADS) Milk secretion. Takahashi (T.), Okayama Igakkwai Zasshi, 1922, No. 394 (Dec.); abst., Jap. Med. World (Tokyo), 1923, 3, 53.

The author concludes that the ovary, especially the one containing the corpus luteum, causes enlargement of the mammary glands and that as soon as the fetus has been delivered, the stimulating substance of the ovary is no longer secreted, the mammary glands begin to contract and milk is secreted. The hormone, which is derived from the fetus and placenta, and which has been generally believed to be the hormone acting directly on the mammary glands, is not a substance which has a direct action on milk secretion. The hormone found in the pregnant blood is unlike that of the fetus and placenta. It is insoluble in either absolute alcohol or ether, but soluble in water and is yellowish white in color. It slightly augments the blood pressure, but does not act on the uterus. It is a simple nitrogenous compound.—R. G. B.

A case of bilateral malignancy of the TESTES. Tanner (C. O.), Calif. State J. (San Fran.), 1923, 21, 55-56.

Report of a case of carcinomatous type of teratoma of the testicle in a man of 4. Due to metastasis the patient died.—I. B.

The results of ligature on the TESTICLE with special reference to the question of the puberty gland (Unterbindungsbefunde am Hoden unter besonderer Berücksichtigung der Pubertätsdrüsenfrage). Tiedje (A.), Ve handl. d. deutsch. path. Gesselsch. (Jena), 1921, 18, 200; see also, Veröffentl. a. d. Kriegs-u. Konstitutions-

pathol., 1921, 2, 1-26; see also, Zentralbl. f. allg. Path. u. path. Anat. (Jena), 1921, 31, 200-201.

See Endocrin., 5, 677.

(GONADS) Does menstruation influence blood concentration? Tyler (M.) & Underhill (F. P.), Am. J. Obst. & Gynec. (St. Louis), 1923, 5, 155-158 (Feb.).

Studies on 11 healthy women, comprising 25 menstrual periods, failed to show a constant variation in the hemoglobin characteristic of any one phase of the menstrual cycle.—E. N.

(GONADS) Gynandroid hermaphroditism complicated by a dermoid cyst of the OVARY (Hermaphroditismo gynandroïde de l'ovaire). Uhlrich (P.), Soc. Anat., 1923 (January 6); abst., Presse méd. (Par.), 1923, 31, 75.

(GONADS) Deficiency symptoms in the menopause due to x-rays (Wegovalverschijnscelen bij Röntgenmenopause). Valken, Nederl Tijdschr. v. Geneesk. (Haarlem), 1922, 66 (II), 2429-2431.

Conclusions are drawn from observations of 100 cases. Vasomotor symptoms are as frequent after castration by operation as by x-rays. Heart symptoms typically caused by x-rays do not exist. After x-ray castration psychical and sexual symptoms are less frequent and not so intense as after castration by surgical procedure. X-rays never completely destroy the ovarian tissue; there always remain traces of endocrine activity; we ought not speak, therefore, of a real castration by x-rays. Ovarian adiposity after x-ray treatment is rare.—J. K.

Atresia of the follicular epithelium of the OVARY in mammals (Atrésie de l'épithélium folliculaire ovarique chez les mammifères). Velloso de Pinho (A.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 830-832.

(GONADS) TESTICLE grafts. Voronoff (S.), Riforma med. (Napoli), 1922, 38, 1017.

Voronoff reports his experiments on animals dating from June, 1917, and on men since June, 1920. Even slices of testicles from cyocephalus monkeys implanted in human testicles gave good results. Although not pretending to explain the whole problem of senility by the atrophy of sexual glands, Voronoff believes that this is the main factor. The results depend very much on the site of the implantation. Voronoff prefers the peritoneum or the tunica vaginalis, because the transudation of plasma can keep up the nourishment of the graft before it is vascularized. Subcutaneous tissue and muscles cannot prevent a central necrosis, and the rest lasts merely for a few months. Voronoff opens the scrotum under local procain anesthesia and fastens the fragments of the implanted testicle at each end with catgut. The glandular surface faces the tunica vaginalis,

which is scarified as well as the tunica albuginea. The fragments must not touch each other. Too small fragments are absorbed. The undivided testicle can be implanted only if it is small and from young animals. (This is stated to be the complete paper prepared for the French Surgical Congress in October. It was debarred from presentation by publication of a summary of it in a daily paper just before the congress.)—J. Am. M. Ass., 80, 66.

(GONADS) Basal metabolism and the menstrual cycle. Wakeham (G.), J. Biol. Chem. (Balt.), 1923, 56, 555-567.

Ninety-eight basal metabolism determinations were made on 24 subjects under exceptional conditions of uniformity. Wakeham concluded that there is a distinct fall in basal metabolism during or immediately after menstruation which is preceded by a rise. Indications are that causes which produce too frequent menstruation are likely to be accompanied by high basal metabolism and that causes which delay or suppress menstruation are likely to be accompanied by a low basal metabolism.—F. S. H.

The histological changes in the OVARY during pregnancy (Ueber die histologischen Veränderung des Ovariums während der Gravidität). Walthard (K. M.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.), 1923, 86, 74-123.

The lipoids of the PLACENTA in the different months of pregnancy. (Ueber die Lipoidssubstanzen der Placenta in verschiedenen Schwangerschaftsmonaten mit besonderer Berücksichtigung ihrer Mengenverhältnisse). Watanabe (H.), Biochem. (Tokyo), 1923, 2, 369-397.

A systematic fractionation of the lipid substances of the placenta showed the presence of phosphatides, lecithin, cephalin, cholesterolin, neutral fats, free fatty acids, and possibly sphingomyelin and a cerebroside. The sex of the fetus has no influence on the distribution of the lipoids. During the course of pregnancy the absolute amounts of lipoids increase, but decrease relative to the growth weight of the fetus. The relation of the neutral fat content of the placenta to the weight of the fetus with development, however, remains practically a constant.—F. S. H.

(GONADS) A contribution to the study of the effects of radium upon rabbit OVARIES. Weis (H. A.), Surg. Gynec. & Obst. (Chicago), 1923, 36, 373-382 (March).

The author's studies lead him to the conclusion that radium in the amount used (600 mg. hours) has no ultimate detrimental effect upon rabbit ovaries. No injurious effect upon the follicles was noted, the ovaries showing a normal histology, with ova in all stages of development. He believes that when radium is given intra-uterinely for menorrhagia, the resulting amenorrhea is not due to the

See Endocrin., 6, 890.

effect on the ovarian follicles, but to the effect on the endometrium, which receives a severe burn from the radium.—E. N.

(GONADS) Histology of the corpus luteum of the human OVARY (Histologie du corps jaune de l'ovaire humain). de Winiwarter (H.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1240-1242.

The influence on the endocrine organs of x-ray treatment of the OVARY (Die Wirkung der Ovarialbestrahlung auf das innersekretorische System). Wintz, *Klin. Wchnschr. (Berl.)*, 1922, 1, 2353.

The influence of x-rays on the ovaries depends on the dosage. A certain dosage produces in effect, castration; when smaller doses are given sterilization is only temporary. This temporary sterilization is often very successful in Graves' disease. The author knows of 35 children born 3-5 years after temporary sterilization of the mother.—J. K.

(GONADS) Therapeutic use of orchitic extract in woman (Thérapeutique orchitique chez la femme). Zénope (B.), *Rev. franç. de gynéc. et d'obst. (Par.)*, 1923, 18, 119-124.

Thirteen patients reacted favorably as regards menstrual and nervous disorders to orchitic extract.—R. G. H.

A rare type of OVARIAN carcinoma (Ueber eine seltene Karzinomform des Ovariums). Zimmerman (R.), *Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.)*, 1923, 86, 19-23.

An exceedingly powerful oxytocic and pressor substance obtained from the posterior lobe of the PITUITARY gland. Abel (J. J.), & Rouiller (C. A.), *Tr. Ass. Am. Physicians (Phila.)*, 1923, May 1-2.

The posterior lobe of the hypophysis has been supposed not to have an internal secretion. Dixon, however, reports that he can find the posterior lobe principle in the spinal fluid and that, injected into an animal, it will increase the substance in the spinal fluid. Byrne also notes that the posterior lobe substance opposes the action of insulin. I believe that we have found that: (1) the posterior lobe principle raises arterial pressure and keeps it up for a long time; (2) it acts on muscle tissue, causing it to contract; (3) it has diuretic action; (4) it constricts the capillaries of warm-blooded and of cold-blooded animals; and (5) it has tonic action on plain muscle tissue. So far we have 2 well known active gland principles—epinephrin and thyroxin. Histamin is the most powerful plain muscle stimulant that we know of, a proportion of 1:200,000,000 causing contraction of the guinea-pig's uterus; but with this posterior lobe substance a proportion of 1:19,750,000,000 will produce the same result, that is, it is 1,250 times as powerful as histamin. We have now reached a point at which the product is 97% pure.

We hope that it will be of use in the isolation of other products, such as insulin and secretin.—J. Am. M. Ass., 80, 1875.

(HYPOPHYSIS, THYROID) The influence of some hormones and proteinogenous amines on the bile-producing ability of the LIVER (Zur Frage der Wechselbeziehungen zwischen innerer und äußerer Sekretion. II. Ueber den Einfluss einiger Hormone und proteinogener Amine auf die Gallenabsonderungsfähigkeit der Leber). Alpern (D.), Biochem. Ztschr. (Berl.), 1923, 137, 507-516.

Dogs were used. Histamin and tenosin increased bile secretion, while pituitrin and thyramin retarded the bile forming ability of the liver. Thyroidin had no definite effect. Atropin acted antagonistically to histamin.—F. S. H.

Le DIABETE INSIPIDE. Ambard (L.) & Lux (H.), Arch. d. mal. d. reins, 1922, 1, 78-97; abst., Ber. ü. d. ges. Physiol. (Berl.), 1923, 16, 233.

Technical study of salt concentration in tissue fluids and blood and salt excretion.—R. G. H.

Differences in the mode of action of **HYPOPHYSEAL** extracts on pregnant and non-pregnant animals (Ueber eine Verschiedenheit in der Wirkungsweise von Hypophysenextrakten bei graviden und nicht-graviden Tieren). Alpern (D.) & Wächter (A.), Arch. f.

in rabbits are reported. In general animal to the injection of pituitary marked and runs a shorter course than that in animal.—F. S. H.

of the **HYPOPHYSIS** (Hypophysentumor). Arlt, Klin. weight of the (Berl.), 1922, 1, 1860.

placenta to that showed symptoms of acromegaly. No other details remains practical.

(GONADS) A con rabbit **OVARIE** Gigantism and stature. Formes frustes of acromegaly. 1923, 36, 373-3 (Gigantisme et haute taille. Cas fruste d'acromegaly).

The author's study. Benard (R.), Bull. et mém. Soc. méd. d. hôp. 1923, 534-542.

upon rabbit ovaries. a patient with acromegaly, unaccompanied by noted, the ovaries show—F. S. H.

of development. He has been reported in the literature in connection with acromegaly (Ueber Zwergwuchs). Berliner (M.), Arch. f. klin. Med. (Berl.), 1923, 2, 126-218; abst., Ber. ü. d. ges.

See Endocrin., 6, 811. 1923, 2, 126-218; abst., Ber. ü. d. ges. 18, 71.

The **HYPOPHYSIS** and hypophyseal syndromes (*L'hypophyse et les syndromes hypophysaires*). Bickel (G.), *Rev. méd. de la Suisse Rom.* (Genève), 1923, 43, 161-171.

A general review of classical data.—R. G. H.

DIABETES INSIPIDUS (*Studi sul diabete insipido*). Biffis (P.), *Policlin.* (Roma), 1922, 29, 286-306; abst., *Ber. ü. d. ges. Physiol.* (Berl.), 1922, 15, 70.

Report on 5 cases with metabolism studies.—R. G. H.

(**HYPOPHYSIS**) Acromegaly. Bonn, *Deutsche med. Wchnschr.* (Berl.), 1923, 49, 533.

Case report.—J. K.

(**HYPOPHYSIS**) Experimental **DIABETES INSIPIDUS** and genital atrophy (*Considérations, sur la pathogénie du diabète insipide et du syndrome adiposo-génitale*). Bremer (F.), *Rev. neurol.* (Par.), 1922, 19, 644-648.

See *Endocrin.*, 5, 761-762.

(**HYPOPHYSIS**) Infundibular polyuria after denervation of the kidneys (*La polyurie tuberienne après épervation des reins*). Camus (J.) & Gournay (J. J.), *Compt. rend. Soc. de biol.* (Par.), 1923, 88, 694-696.

Complete denervation of the kidneys before or after a lesion of the base of the brain does not prevent the polyuria resulting from such a lesion.—T. C. B.

The functions attributed to the **HYPOPHYSIS** (*Les fonctions attribuées à l'hypophyse*). Camus (J.) & Roussy (G.), *J. de Physiol. et de path. gén.* (Par.), 1922, 20, 509-518.

A review and elaboration of the work of these authors, which, now confirmed by Houssay and by Bailey and Bremer, leads to depriving the hypophysis of functions which have been attributed to it, and crediting the effects of experimental and pathological disturbance of the region to effects on the base of the brain nearby.

—W. B. C.

The functions attributed to the **HYPOPHYSIS** (*Les fonctions attribuées à l'hypophyse*). Camus (J.) & Roussy (G.), *J. de Physiol. et de path. gén.* (Par.), 1922, 20, 535-547.

In this article the authors have brought forward anatomical and pathological evidence further supporting their view that injury to the region of the tuber cinereum is the cause of symptoms formerly and erroneously attributed to injury of the hypophysis.—W. B. C.

HYPOPHYSEAL syndromes (*Les syndromes hypophysaires. Anatomie et physiologie pathologiques. Rapport*). Camus (J.) & Roussy (G.), *Rev. neurol.* (Par.), 1922, 29, 622-639.

See *Endocrin.*, 6, 890.

The rôle of the posterior lobe in the glandular function of the **HYPOPHYSIS** (*Sur le rôle du lobe postérieur dans la fonction glandulaire de l'hypophyse*). Celestino da Costa (A.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 833-835.

Radium in tumors of the HYPOPHYSIS. Charles (J. W.), *Progr. Med. (Phila.)*, 1921, 2, 377.

The author quotes Quick in discussing the advantage of radium over the x-ray in the treatment of hypophyseal tumors. The nicety, as well as intimacy of application is in favor of radium. The pituitary is enclosed in a bony box and from some portals of entry interposed crests of bone add to the filtration and scattering of the x-rays; irradiation over such a wide area may permanently damage the retina. Radium, on the other hand, can be applied under proper filtration by the intranasal route directly to the hypophysis.—I. B.

PITUITARY preparations (*La matière médicale des préparations hypophysaires*). Choay (A.), *Presse méd. (Par.)*, 1923, 31, 123-124.

Details of comparative anatomy are given about the hypophysis in cattle, horses, sheep and hogs, as these animals furnish the material for pituitary preparations. Whereas the average weight of the pituitary in man is 0.35-0.45 gm. according to Testut, the weight of the glands used as *materia medica* is as follows: cattle, 100-300 gm., according to the size of the animal; horses, average 1.80 gm.; sheep, 0.60 gm. and hogs, 0.22 gm. The anterior and the posterior lobes in the pituitary of cattle can be readily separated and form the basis of single-lobe preparations; the separation of the two lobes in horses and sheep is complicated and requires great skill, so that these glands can be used only for the manufacture of whole-gland preparations. The relative amounts of desiccated material obtained from the pituitary of the 4 types of animals in question is as follows: of the fresh gland of cattle, 2.20 gm. yields 0.48 gm.; of horses, 1.80 gm. gives 0.36 gm.; of sheep, 0.60 gm. gives 0.13 gm. and of hogs, 0.22 gm. yields 0.05 gm.; the amounts of desiccated substance obtained from 1.80 gm. of anterior beef pituitary is 0.40 gm., and from 0.40 gm. posterior lobe about 0.08 gm.—G. L.

(**HYPOPHYSIS**) A case of dwarfism. Cockayne (E. A.), *Brit. J. Child. Dis. (Lond.)*, 1922, 19, 36.

The colloid spaces in the connective tissue of the **HYPOPHYSIS** in man (*Les lacunes colloïde dans le tissu conjonctif de l'hypophyse chez l'homme*). Collin (R.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 92-93.—T. C. B.

Cytology of HYPOPHYSIS (Sur la fonte holocrine des cellules hypophysaires chez l'homme). Collin (R.), *Compt. rend. Soc. de biol. (Par.)*, 1922, 87, 1206-1208.

Histological.—T. C. B.

Treatment of tumors of the HYPOPHYSIS (Zur Behandlung der Hypophysentumoren). Denker, *Internat. Zentralbl. f. Ohrenh. (Leipz.)*, 1921, 10, 97.

See *Endocrin.*, 6, 892.

The HYPOPHYSIS following brain lesions (L'ipofisi nelle lesioni del cervello). Desogus (V.), *Riv. di biol. (Torino)*, 1922, 4, 515-520; see also, *Schweiz. Arch. f. Neurol. & Psychiat. (Zürich)*, 1922, 11, 244-260.

See *Endocrin.*, 6, 709.

PITUITARY secretion. Dixon (E. W.), *J. Physiol. (Lond.)*, 1923, 57, 129-138.

Difference of opinion as to the presence of pituitrin in the cerebro-spinal fluid led to the experiments described in this paper. It is concluded that the pituitary secretes into the cerebro-spinal fluid. Pituitary extract injected into the circulation causes the gland to secrete. Ovarian extract specifically excites secretion. Pituitary extract increases the tone of the small intestine, but diminishes the tone of the large intestine.—T. C. B.

On the active principles of the PITUITARY gland. Dudley (H. W.), *J. Pharmacol. & Exper. Therap. (Balt.)*, 1923, 21, 103-122.

A crystalline picrate was obtained from the posterior lobe of the pituitary which produced effects on smooth muscle and blood pressure that were similar to the effects of the pituitary extracts and which showed an activity of the same order as that induced by histamine. The substances proved to be potassium creatinine picrate contaminated with small amounts of pituitary principles. Two principles were obtained from this: an acetone insoluble "A" an acetone soluble "B" fraction. "A" produced uterine contractions in a dilution of 1 part in 1,250,000,000 and showed an uncomplicated pressor action. "B" had one-twentieth the oxytocic activity of "A" and produced a strong depressor action followed by a moderate pressor effect. Evidence is given to show that the oxytocic and pressor principles of "A" are two separate substances and that the pressor actions of "A" and "B" are produced by different chemical entities.

—G. E. B.

(HYPOPHYSIS) Neuropsychiatric sequelae of acute epidemic encephalitis in children. Ebaugh (F. G.), *Am. J. Dis. Child. (Chicago)*, 1923, 25, 88-98.

In 17 cases of post-encephalitic disturbances in children, one child showed endocrine changes. There was a general increase in

distribution of fat, especially marked in the pelvic region, showing hypopituitarism. She also showed a tendency to exophthalmus which may have indicated thyroid activity to compensate for the hypopituitarism. There was increased sugar tolerance, basal metabolism of plus 16 and a normal sella turcica.—M. B. G.

(HYPOPHYSIS) Retinitis pigmentosa and dystrophia adiposogenitalis. Elschnig-Biedl, München. med. Wchnschr., 1922, 69, 1138.

A case of diffuse HYPOPHYSITIS (Ein Fall von akuter diffuser Hypophysitis). Fahr, Deutsche med. Wchnschr. (Berl.), 1923, 49, 497.

A girl of 15 died from sepsis which originated from furunculosis. In the hypophysis a purulent inflammation was found.—J. K.

Influence of PITUITRIN on cerebrospinal fluid. Fujino (R.), Chugwai Iji-Shimpo, 1922, No. 1024 (Nov.); abst., Jap. Med. World (Tokyo), 1923, 3, 32.

Subdural injection of 0.3-0.7 cc. of pituitrin caused a rise in cerebrospinal pressure but no other change, while in progressive paralysis, tabes dorsalis and syphilis of the central nervous system there was a decrease in the pathological contents of the cerebrospinal fluid.—R. G. B.

Action of HYPOPHYSEAL extracts on gastric contraction (Acción de los extractos de hipofisis sobre la motricidad gastrica). Galan (J. C.), Rev. Asoc. méd. argent. (Buenos Aires), 1921, 34, 20-23 (Sec. Soc. de Biol.).

Strong doses of hypophyseal extract cause contraction. There is an increase in the strength and frequency of the contractions with weak doses. On the isolated stomach of the frog, toad, rat, cat and dog the inhibition sometimes noted is due to chloretone (in pituitrin). In the dog there is brief inhibition in the pylorus and antrum, then long lasting augmentation.—B. A. H.

A special lobe of the HYPOPHYSIS cerebri in embryo sheep and its significance (Su uno speciale lobulo dell' hypophysis cerebri in embrioni di pecora e sul suo significato). Ganfini (C.), Arch. ital. di anat. e di embriol. (Firenze), 1922, 19, 95-121.

Largely an embryological study based on 17 sheep embryos from 12 mm. in length to embryos 5 months old. An extension of the pars intermedia into the anterior lobe is described. Of morphological interest only.—A. T. R.

The action of posterior HYPOPHYSIS extract on urinary secretion (Etude expérimentale de l'action de l'extrait d'hypophyse postérieure sur la secretion urinaire). Garnier (M.) & Schulmann (E.), Rev. neurol. (Par.), 1922, 640-643; abst., Ber. ü. d. ges. Physiol. (Berl.), 1923, 16, 254.

Extracting the lipoids with chloroform did not diminish the antidiuretic property of hypophyseal extract.—R. G. H.

Cutaneous alterations in the toad after removal of the **HYPOPHYSIS** (*Modificaciones cutáneas del sapo privado de hipófisis*). Giusti (L.) & Houssay (B. A.), *Rev. Asoc. méd. argent.* (Buenos Aires), 1921, 34, 96-100 (Sec. Soc. de Biol.).

See *Endocrin.*, 6, 312.

The rôle of the **HYPOPHYSIS** and of the brain in the production of cutaneous alterations in the toad (*Influencia de las lesiones de la hipófisis y del cerebro sobre las alteraciones cutáneas de los sapos*). Giusti (L.) & Houssay (B. A.), *Rev. Asoc. méd. argent.* (Buenos Aires), 1922, 35, 42-47 (Sec. Soc. de Biol.).

See *Endocrin.*, 7, 173.

(**HYPOPHYSIS**) Clinical studies. Graves (M. L.), *South. M. J.* (Birmingham), 1923, 16, 152-160.

History of a case of hypophyseal disorder.—J. C. D.

(**HYPOPHYSIS**) Vegetative centers in the hypothalamus (*Zur Anatomie, Physiologie und Pathologie der vegetativen Zentren im Zwischenhirn*). Greving (R.), *Ergebn. d. Anat. u. Entwicklungsgesch.* (Berl.), 1923, 24, 348-413.

An extended review of the anatomy, physiology and pathology of the hypothalamic region of the brain, where certain vegetative centers are supposed to be located. The article is of some endocrine interest because a number of symptoms generally associated with hypophyseal disturbances may be due to involvement of neighboring brain centers. An extensive list of references is given.—A. T. R.

Defects in the membranous bones, **DIABETES INSIPIDUS** and exophthalmus, with report of a case. Grosh (L. C.) & Stifel (J. L.), *Arch. Int. Med.* (Chicago), 1923, 31, 76-83.

A queer case, the seventh in the literature, with syndrome indicated in the title. Dwarfism was also a feature. The etiology of this disease is unknown. Syphilis, tuberculosis, osteitis fibrosa, Paget's disease, bone cysts, and malignant diseases could be excluded.—H. L.

DIABETES INSIPIDUS. A case report following epidemic encephalitis with enormous polyuria. Hall (G. W.), *Am. J. M. Sc.* (Phila.), 1923, 165, 551-562.

An excellent review of the literature is included.—R. G. H.

(**HYPOPHYSIS**) Myxedematous dyspituitarism. Hastings (J. P.), *Med. J. Australia* (Sydney), 1922, ii, 526-527.

Report of a case in a 45 year old woman who became hallucinated following a goiter operation. Subsequently she developed acromegalic manifestations.—R. G. H.

(HYPOPHYSIS) Dystrophia adiposo-genitalis in a leper [Dystrophie adiposogenitale (syndrome hypophysaire adiposo-génital) chez un lépreux]. Hirschberg, Bull. Soc. path. exot. (Par.), 1923, 16, 75-77.

First case report of a patient exhibiting the two diseases mentioned in the title. The possibility that the condition may be analogous to the endocrine disturbances of syphilitic origin is expressed.

—F. S. H.

The effect of PITUITARY (anterior lobe) injection upon normal and THYROIDECTOMIZED Axolotls. Hogben (L.), Proc. Roy. Soc. Lond., 1923, 94B, 204-215.

Injection of desiccated anterior lobe extract produced metamorphosis in sexually mature Axolotl larvae with a rapidity comparable to that induced by thyroid administration, while pituitary feeding was without influence. After thyroidectomy the extract was still capable of inducing metamorphosis. Transplantation of the thyroids from a large Axolotl into a smaller subject was without effect. Spontaneous metamorphosis does not occur in Axolotls remaining in shallow water.—G. E. B.

Colour response in the HYPOPHYSECTOMIZED frog. Hogben (L. T.) & Winton (F. R.), Proc. Roy. Soc. (Lond.), 1923, 95B, 15-31.

Extracts of the posterior lobe of the pituitary gland of mammals, birds, reptiles, amphibians and fishes have a specific local action on the melanophores of the frog, bringing on maximal expansion both in the intact animal and in isolated strips of skin. Sufficient extract may be obtained from the pituitary of a single frog to produce darkening in more than 50 other subjects. This melanophore stimulant resembles in certain biochemical properties the oxytocic principle of the pituitary. Removal of the anterior lobe in the frog does not affect its pigmentary response to natural factors while after the removal of the whole gland complete melanophore contraction is maintained even when the animal is exposed to natural factors that bring on melanophore expansion in the normal animal. Melanophore expansion is induced in hypophysectomized frogs by injection of post-pituitary extracts.—G. E. B.

PITUITARY gland dystrophies. Hollander (L.), Arch. Dermat. & Syph. (Chicago), 1923, 7, 632-636.

A note on 2 cases of dystrophia adiposo-genitalis and 1 with ill defined symptoms and a distorted sella.—J. C. D.

Influence of the HYPOPHYSIS on growth (Influencia de la hipofisis sobre el crecimiento). Houssay (B. A.) & Hug (E.), Rev. Asoc. méd. argent. (Buenos Aires), 1921, 34, 269 (Sec. Soc. de Biol.).

Experiments were performed on 11 lots of puppies. Extirpation of the hypophysis caused arrest of growth, dental alterations, diminution of the thyroid (very thin epithellum), atrophy of the thymus, atrophy, frequently, of the testes, adiposity, etc. Incomplete ablation impeded growth little or none. Opothorapy was inefficacious

—B. A. H.

(HYPOPHYSIS, GONADS) Differential diagnosis between retarded eunuchoidism and dystrophia adiposogenitalis (*Zur Differentialdiagnose des Späteunuchoidismus und Dystrophia adiposogenitalis*). Hueck (W.), München. med. Wchenschr., 1922, 60, 1507-1508.

A man of 27 years suffered for 5 years from headache, giddiness and palpitations. As time went on he became weaker and his testicles decreased in size. The sella was large. The fat was of typically eunuchoid distribution. The nails were normal. He was quiet but without the dullness characteristic of hypothyroidism. The quantity of blood sugar was normal. He was very sensitive to pilocarpin. The author believes that the patient had Frölich's disease, caused by a hypophyseal tumor, although symptoms of increased brain pressure were absent. This, however, is not rare in pituitary tumors.—J. K.

(HYPOPHYSIS) Diagnosis and treatment of nocturnal and diurnal enuresis. Jacobs (F. B.), Penn. M. J. (Harrisburg), 1922, 25, 867-869.

Eleven girls and 29 boys suffering from enuresis were given 0.5 to 1 cc. of posterior lobe pituitary extract (obstetrical variety) subcutaneously, once weekly for 3 to 5 doses. Of the 49 subjects treated, 17 were greatly improved, 16 were cured, and 16 unimproved. A period of 3 months has elapsed in most of the cases reported as cured. In the cases reported as greatly improved, the enuresis has been cut from a nightly occurrence mostly, to once a week, and in many cases, to once or twice in 12 weeks.—H. L.

A rare case of syphilis of the central nervous system combined with an HYPOPHYSEAL lesion (*Ueber einen seltenen Fall von Lues des Zentralnervensystems, kombiniert mit einer Erkrankung der Hypophyse*). v. Josephy (H.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.), 1920, 58, 56-78.

A 53 year old woman had a still-born child. The clinical findings were: optic atrophy, pupillary disturbance, convulsive seizures, attacks of unconsciousness, speech disturbance, spastic and flabby paresis, mental lapse, restlessness, disorientation and confabulation. The Wassermann test of the blood was negative, of the spinal fluid, incompletely positive. The disorder was slowly progressive in course and without fluctuations. It was first diagnosed as tabes, then paralysis and finally as a syphilitic lesion of the brain, the latter

based on further observation of a pseudobulbar paralytic picture. Besides several large gummata in the right temporal lobe, there were diffused small 'granuloma in the cerebellum pons, oblongata and spinal cord;' also military gummata or accumulations of epithelioid cells, with lymphocytic foci and surrounding perivascular infiltrations were found. There was a general syphilitic leptomeningitis with a tendency toward nodule formation. Small gummata on the inner side of the spinal dura were observed, but no diffused brain lesions, especially none that would have caused paralysis, were seen. Spirochetes could not be detected. Disseminated military gummata of the central nervous system have, up to this time, been described only as attendant phenomena of paralysis (Sträussler, Jacob and others). Besides these disorders there were extensive and peculiar changes in the enlarged hypophysis; this had produced no clinical symptoms, and probably exhibited a peculiar histological form of syphilis. An identical condition was found by Simmonds in 4 cases, but these were not diagnosed as syphilitic.—R. G. H.

(HYPOPHYSIS) Pathology of salt metabolism (*Zur Pathologie des Salzstoffwechsels*). Jungmann (P.), *Klin. Wchnschr. (Berl.)*, 1923, 2, 18-19.

Report of a case. A man of 44 complained of gradual loss of appetite, dullness, headache and the symptoms of diabetes insipidus. NaCl excretion was apparently normal; water excretion was nearly normal. This would, according to the author, exclude the diagnosis of diabetes insipidus. Analysis of the blood showed that the NaCl metabolism was normal only in appearance; even when the diet was low in NaCl there existed hyperchloremia, and the freezing point was 0.62, a proof of hyperosmosis of the serum. The skiagram showed a large sella with bone structure such as is caused by low calcium. Autopsy showed an abscess in the hypophysis. The bones of the sella were almost as thin as a sheet of paper. Microscopically, the hypophysis showed only a small quantity of normal glandular tissue at the periphery; the rest consisted partly of inflamed tissue, partly of a cavity caused by the formation of the abscess. The medulla of the adrenals was normal, but there was only a small quantity of cortex. After a discussion of the different theories concerning the pathogenesis of diabetes insipidus, the author states that the hypophyseal origin of diabetes insipidus has not been proved, that the centers regulating water and salt metabolism may undergo pathological changes, thus producing the disease. As there is more than one center the different forms of diabetes insipidus (with hyperchloremia, hypochloremia, etc.), the author suggests, might be attributed to different anatomical lesions.—J. K.

The effect of PITUITRIN upon the blood pressure and diuresis.
Kasa, (T.), *Tohoku Igakukai Zasshi (Sendai)*, 1922, 6, 41-71.

In order to examine the effect of pituitrin on sympatheticotonic and vagotonic men, adrenalin, pilocarpin, and pituitrin were injected subcutaneously, and changes in the blood pressure, the amount of nitrogen and salts in urine and its total quantity were determined. In men sensitive to adrenalin, the injection of pituitrin never increases the blood pressure, but excites the urine discharge. In men insensitive to adrenalin, the results are diametrically opposite. An administration of 500 to 700 cc. of warm water before injection prevents the diuretic action of pituitrin, and diminishes the concentration of nitrogen and salts in the urine. From these results the author concludes that the pituitary body contains only one substance but that this may act on the blood pressure in different ways according to the different conditions of the nervous system. If the subject is put into a condition of polyuria, the injection of pituitrin prevents diuresis for 3 to 4 hours, as is seen in diabetes insipidus. The pituitary body seems, therefore, to be an organ which controls the water content of the body.—S. K.

HYPOPHYSEAL disease probably of syphilitic origin. Key (B. W.), *Am. J. Ophth.* (Chicago), 1922, 5, 956-961; cit., *J. Am. M. Ass.* (Chicago), 1923, 80, 59.

PITUITRIN diuresis in diseases of the kidney (*Über den Ablauf der Pituitrin diurese bei Nierenkranken*). Klein (O.), *Wien. Arch. f. inn. Med.*, 1923, 5, 429-450.

When pituitrin is injected into patients with diseases of the kidney the type of diuresis depends largely upon the anatomical lesion of the kidney, especially upon the quantity of normally functioning kidney tissue still in the body and the likelihood of the patient's getting edema. Insufficiency of the kidneys causes retardation of the pituitrin reaction, but specific gravity, the water content of the blood, etc., undergo the same changes in patients with abnormal kidney function as in normal persons, although the reaction is slower after the injection of extract of the posterior lobe of the hypophysis. In patients who are very apt to get edema, hydremia, a normal reaction after pituitrin administration, may not occur, and secondary diuresis of water may not be seen. However, the injection of pituitrin in a patient with a renal disorder may be an excellent clinical method of estimating the degree of the renal and extrarenal disturbances existing at a certain moment.—J. K.

HYPOPHYSIS and adiposity (*Hypophyse und Fettsucht*). Knipping (H. W.), *Deutsche med. Wchnschr.* (Berl.), 1923, 49, 12-13.

The author studied 15 cases of adiposity and experimented on dogs in which the anterior lobe of the hypophysis was destroyed. The results indicate that the hypophysis has a most important part in the regulation of metabolism. The normal gland regulates oxydation after ingestion of food. This function is lost when large parts

of the organ lose their normal function and adiposity occurs. In many patients the sexual functions are markedly diminished also. Oral administration of hypophysis may prove of much value.—J. K.

Comparative anatomy of the HYPOPHYSEAL membranes (Zur Vergleichenden Anatomie der Hypophysenumgebung). Koller (R.), *Ztschr. f. Anat. u. Entwicklungsgesch.* (Berl.), 1922, 65, 183-203.

(HYPOPHYSIS) Case of Dercum's disease (Un cas de maladie de Dercum). Laignel-Lavastine & Largeau (R.), *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1923, 47, 665-667.

Case report. The basal metabolism was normal.—F. S. H.

(HYPOPHYSIS) Gigantism or precocious macrosomia (Gigantisme ou macrosomie précoce. Soudure prématurée des cartilages de conjugasion). Léri (A.) & Leconte, *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1923, 47, 327-331.

Presentation of the case of a child of 6 years. The body size was normal for that of 12 or 13 year old boy and the ossification and epiphyseal state was consonant with the size and not the age.

—F. S. H.

Three cases of HYPOPHYSEAL cachexia (Drei Fälle von Simmondscher Krankheit). Lichtwitz (L.), *Klin. Wchnschr.* (Berl.), 1922, 1, 1877-1879.

The case is reported of a man of 21. Two years before the report his disease began with extreme thirst and polyuria. The diagnosis, diabetes insipidus was made. The patient became feeble and dull. The beard did not grow; libido disappeared; the sex organs atrophied; there was loss of hair in pubes and axillae and the patient showed a marked growth in height. The blood pressure was 100 mm. Hg. Wassermann examination was negative. Skiagram of the skull showed a slightly enlarged sella with 3 suspected spots, resembling material rich in calcium. Injections of pituglandol, combined with x-ray treatment of the sella produced no outward improvement, although the patient said he felt better. A woman of 31 who had formerly undergone treatment for syphilis and diabetes insipidus was observed. Menstruation had stopped 8 years before; she lost all body hair and sexual desires were no longer manifest. There was atrophy of the sex organs. The sella did not seem enlarged, but the radiogram showed an abnormal spot in the posterior part of the sella which probably contained a large amount of calcium. A woman of 41 had been treated for syphilis. The thyroid was hard; the hair was almost entirely gone and the sex organs had atrophied. A very large sella was seen with crooked pro- and post-clinoids and the same sort of abnormal spots as were

described in the preceding cases. The first case, especially, is interesting, as hypophyseal cachexia in men is rare.—J. K.

DYSPITUITARISM and epilepsy. A report of six cases. Lissner (H.) & Nixon (C. E.), *Med. Clin. N. Am. (Phila.)*, 1923, 6, 1471-1490.

An interesting and valuable discussion of "Idiopathic" epilepsy associated with evident endocrine, especially pituitary, dysfunction. In one of the cases reported the facies and x-ray examination indicated acromegalic changes in addition to changes in the visual fields. The sella in the other 5 subjects was probably within normal limits. Except in the acromegalic, obesity was quite marked in all; this was of the girdle type, pathognomonic of hypopituitarism. Five of the 6 patients reported had reached or passed puberty, and all presented menstrual disturbances especially characterized by a scanty flow and an abnormally prolonged interval. All 6 subjects presented hair changes suggestive of hypothyroidism, and the velvety, smooth, cold, waxy skin indicating deficient pituitary function. In one subject changes in hair distribution of heterosexual type were present. The basal metabolism in the acromegalic patient was +15%, in another with evident hypothyroidism it was -21%, in the remaining 4 subjects the metabolic rate was normal. Mental retardation, especially impaired memory, was fairly marked in all except one subject; emotional disturbances commonly seen in endocrine dysfunction were noted in all six. Organotherapy was administered to all 6 patients with strikingly beneficial results in the menstrual disturbances, obesity and mental and emotional status. In the 5 patients under treatment for a long enough period of time epileptic seizures either ceased entirely or became far less frequent and much milder. Two of these 5 patients received no sedatives. The authors emphasize the importance of early apprehension and treatment of endocrine abnormalities. Treatment should be continued over many months or even years. Patience is a vital requirement in all gland therapy, and no results can be expected from haphazard, briefly applied treatment.—I. B.

The use of **HYPOPHYSIS** extracts and sublimate by mid-wives (*De l'emploi par les sages-femmes des extraits hypophysaires et du sublimé*). Le Lorier, *Bull. Soc. d'obst. et de gynéc. (Par.)*, 1923, 12, 12.

Prohibition of the use of hypophyseal extracts by mid-wives is advocated.—F. S. H.

General infantilism of endocrine origin, probably hypofunction of the **HYPOPHYSIS** (*Universeller Infantilismus aus innersekretorischer Ursache wahrscheinlich Hypofunktion der Hypophysis*). Löwe, *Deutsche med. Wchnschr. (Berl.)*, 1923, 49, 102.

No details are given.—J. K.

(**HYPOPHYSIS**) Dwarfism (Ein Fall echter Nanosomie). Mau, Klin. Wchnschr. (Berl.), 1922, 1, 1972; see also, München. med. Wchnschr., 1922, 69, 1133.

The case is reported of a boy of 12 years, 100 cm. in height who was well proportioned and of excellent intelligence; skiagram showed a defect in the sacrum; anisocoria, pes equinus and atrophy of the right testicle were also observed. Thyroid function appeared normal.—J. K.

(**HYPOPHYSIS**) Syndrome adipo-génital avec selle turcique normale. Mouriquand, Ravault (P.) & Chassard, Soc. méd. d. hop. de Lyon, 1923 (January 9); abst., Presse méd. (Par.), 1923, 31, 76.

Pathological findings of Dr. Sagaro's case of **DIABETES INSIPIDUS**. Nakamuro (H.), Juzenkwaï Zasshi, 1922, 27, No. 4 (April); abst., Jap. Med. World (Tokyo), 1922, 2, 266.

The author observed hemorrhage and an inflammatory condition about the base of the cerebrum and believed this to be the cause of the diabetes.—R. G. B.

(**HYPOPHYSIS**) The biological assay of **PITUITARY** extract. Nelson (E. E.), J. Lab. & Clin. M. (St. Louis), 1923, 8, 318-333.

A valuable contribution to the subject of the standardization of endocrine products which does not lend itself to abstracting and should be read in its entirety to be appreciated. The author concludes by stating that a definite recommendation will be made very shortly as to the details of preparation of a standard from the pituitary gland itself, together with the details of the exact method to be followed in the biological assay of pituitary extract.—I. B.

Hemophilia and **PITUITARY** extract. Neumann (H.), Med. Klin. (Berl.), 1923, 19, 115.

Neumann reports a case of probable hemophilia. The bleeding from the nose stopped after one local and one subcutaneous application of pituitary extract.—J. Am. M. Ass., 80, 1277.

The **HYPOPHYSIS** in Raynaud's disease (La maladie de Raynaud et l'hypophyse). Nicolis (N.), Radiol. méd., 9, 118; J. de radiol. et d'électrol. (Par.), 1922, 6, 433.

The author has radiographed the hands, lower extremities of the forearm, the cervical vertebra, and the hand of a patient suffering from local asphyxia of the extremities. He found no lesion of the bones of the hand, no apparent calcification of the radial or ulnar arteries, and no cervical ribs, but in focusing the rays on the sella turcica he was surprised to find the "pineal" gland calcified and the sella turcica enlarged.—Med. Sc., 8, 83.

(HYPOPHYSIS) Unknown formation of cataract in a boy of 10 with **DIABETES** (Bisher nicht bekannte Kataraktbildung bei einem 10 jährigen Diabetiker). Pick, Deutsche med. Wchnschr. (Berl.), 1922, 48, 1692.

The case is reported of a boy with diabetes who had opaque spots in the shape of points in the lenses. The vision improved markedly upon administration of hypophysis tablets.—J. K.

A case of infantilism, hypofunction of the **HYPOPHYSIS** and congenital mitral stenosis (Sopra un caso di infantilismo da ipofunzione ipofisaria e da stenosi mitralica congenita). Poggio (G.), Glor. di clin. med. (Parma), 1923, 4, 2-13.

A critical analysis of an interesting case of infantilism due to primary hypophyseal lesion, accompanied by a secondary pluriglandular syndrome (thyroid, testicle, adrenals) and by partial visceral hypoevolution (mitral stenosis).—P. N.

Dystopia of the NEUROHYPOPHYSIS (Ein weiterer Beitrag zur Kenntnis der Dystopie der Neurohypophyse). Priesel (A.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1922, 70, 209.

Reference has already been made to a case of dwarfism investigated by the author which was due to dystopia of the posterior lobe of the pituitary body. He has now observed two further cases of a similar dystopia in otherwise normally built subjects. The cases are, however, important as no similar ones appear to have been so far described.—Med. Sc., 8, 61.

Pathology of the HYPOPHYSIS (Zur Pathologie der Hypophyse). Reinhardt, Klin. Wchnschr. (Berl.), 1922, 1, 2309.

A short note on hypophyseal cachexia and its importance in pathology. No new data.—J. K.

DIABETES INSIPIDUS or **HYPOPHYSEAL** polyuria. Riely (L.), J. Oklahoma M. Ass. (Muskogee), 1921, 14, 276-277.

A case record of a man of 34 with polyuria presumably of hypophyseal origin.—W. J. A.

Tethelin: A growth-controlling substance obtainable from the anterior lobe of the **PITUITARY** body. Robertson (T. B.), Biochem. J. (Lond.), 1923, 17, 76-82.

A polemical reply to the criticism and experiments of Drummond and Cannan (Biochem. J., 1922, 16, 53). Robertson upholds his earlier experimental work in this paper to the satisfaction of thoughtful investigators.—F. S. H.

Tumor of the HYPOPHYSIS (Syndrome tubéro-hypophysaire avec cécité, infantilisme, état adiposogénital, oligurie; tumeur visible à la radiographie). Roger (H.), Pourtal (L.) & Sedan, Comité

(H.), Kornfeld (F.), & Weissbarth (E.), *Klin. Wchnschr. (Berl.)*, 1922, 1, 2238.

When patients with tetany ingest HCl, less acid is excreted than in normal persons; on the contrary, more acid is excreted after the ingestion of NaCl. Many subjects retain acid as well as ammonia; in these patients the excretion of water, chlorine and phosphorus is also retarded.—J. K.

(PARATHYROID) Postoperative tetany with epilepsy, and its treatment (Postoperative Tetanie mit epileptischem Anfall, zugleich zur Frage der Therapie). Graef (W.), *München. med. Wchnschr.*, 1922, 69, 1119-1120.

A woman of 24, suffering from oppressed respiration caused by a goiter, was operated upon. Three days after the operation the first tetanic contraction was seen. Then permanent tetany developed, ending after a month with an epileptic fit. Administration of parathyroid extract seemed to have little or no influence. The best results were obtained with calcium preparations and narcotics.—J. K.

(PARATHYROIDS) Inorganic ion ratio after administration of oxalates and citrates. Gross (E. G.), *J. Biol. Chem. (Balt.)*, 1923, 55, 729-738.

Determination of the chlorine, phosphorus, calcium, potassium, sodium and magnesium ion concentration of the blood of dogs to which sodium oxalate or sodium citrate had been administered and a comparison of the results with the findings in parathyroid tetany. The subcutaneous injection of sodium oxalate produces tetany with a marked disturbance in the blood salts. The sodium, chlorine and calcium are decreased, while total phosphorus and potassium are increased, magnesium remains singularly constant. Sodium citrate produced none of these changes.—F. S. H.

(PARATHYROIDS) Discussion on "the present position of organo-therapy." Grove (W. R.), *Proc. Roy. Soc. Med. (Lond.)*, 1923, 16, 18-22. (Sec. Therap. & Pharmacol.)

The author's deductions are based on his previous observations to the effect that calcium salts, administered either by mouth or intramuscularly, stimulate the reparative processes. It was found that chronic varicose ulcers of the leg are associated with marked reduction of the patient's blood calcium, and that raising the calcium content leads to marked improvement of the ulcers. Subsequently it was discovered that parathyroid in doses of 1/10 gr. by mouth rendered the calcium blood content normal with resulting cure of the ulcers. Ulcers which resisted this mode of treatment were found to be associated with infectious foci in teeth and elsewhere, the removal of which resulted in startling improvement and prompt cure through parathyroid treatment. In the absence of in-

fectious foci, even gastric and duodenal ulcers, acute phlebitis, bed sores, the various forms of arthritis, severe burns, sciatica, and even such conditions as pericarditis, nasal infections, gumma of the face, herpes zoster of the conjunctiva with iritis, pernicious anemia, and hypertrophy of the prostate, all of which were associated with demonstrable calcium deficiency, were markedly benefited by parathyroid administration. Calcium deficiency appears to be an index of the absorption of a toxin, and many chronic diseases are due to the breakdown of the defenses of the body in controlling this mechanism, which is apparently situated in the parathyroid glands. The author affirms that parathyroid is not a cure; it is merely a physiological aid to the healing of chronic lesions due to toxic absorption; if the focus of this toxin be removed, parathyroid extract will then bring about a cure. If the focus cannot be removed it is a valuable remedial agent, though not a cure.—I. B

Elementary chemical study of PARATHYROID glands of cattle. Hanson (A. M.), Mil. Surgeon (Wash., D. C.), 1923, 52, 280-285; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1341

Lattice fibers in the PARATHYROID (Über "Gitterfasern" im Epithelkörperchen und deren Genese). Koritschoner (R.), Ztschr. f. Anat. u. Entwicklungsgesch. (Berl.), 1922, 60, 404-423.

Of morphological interest only.—A. T. R

Treatment of postoperative tetany by grafting of PARATHYROID glands of horses (Behandlung der postoperativen Tetanie durch Ueberpflanzung von Pferdeepithelkörperchen). Krecke, München. med. Wehnschr., 1922, 60, 1129.

PARATHYROID and paralysis agitans. Kuhl, Deutsche med. Wehnschr. (Berl.), 1923, 49, 497.

A case is reported in which a patient with Parkinson's disease was apparently cured by implantation of a parathyroid.—J. K.

The function of the PARATHYROID. Salvesen (H. A.), J. Biol. Chem. (Balt.), 1923, 56, 443-456.

From a series of partially and completely parathyroidectomized dogs on which determination of the calcium, phosphorus, blood sugar, and alkali reserve of the blood were made and a study of the calcium excretion in urine and feces, Salvesen comes to the conclusion that the symptoms of parathyroid insufficiency are due to calcium deficiency. The belief is expressed that the parathyroids control the calcium level of the blood and by so doing they influence the function not only of the muscle and the nerve tissue, but probably of all the organs. The tetany which occurs in dogs, when they are transferred from a milk diet to a meat diet, is not due to the meat, as such, but to the lack of calcium in the diet which was formerly supplied by the milk—F. S. H.

(PARATHYROID) Otitis fibrosa. Sauer, Klin. Wchnschr. (Berl.), 1922, 1, 2357.

Giant cell sarcoma (Virchow), bone cysts and epulis are all special forms of otitis fibrosa. Pathogenesis is unknown but more and more cases are published in which changes in one of the parathyroids, especially adenomas, are found, leading some investigators to believe that the disease is caused by increased calcium metabolism. These investigators recommend the ablation of the pathological parathyroid.—J. K.

(PARATHYROIDS) Tetany in the adult with special reference to alkalosis and calcium metabolism. Tileston (W.) & Underhill (F. P.), Tr. Ass. Am. Physicians (Phila.), 1922, 37, 87-99.

The action of the blood serum of animals in **TETANIA PARATHYREOPRIVA** on motor nerve and muscle. Yoshimoto (M.), Quart. J. Exper. Physiol. (Lond.), 1922, 13, 41-53.

The serum of thyro-parathyroidectomized cats and dogs increases the excitability of isolated frog's nerve, but has no effect on muscle. A solution of guanidine carbonate, 0.01%, also increases the excitability of the nerve.—T. C. B.

The **PINEAL** body. Funk (E. H.), Progr. Med. (Phila.), 1921, 2, 325-327.

A review of the clinical phenomena associated with derangements of pineal structure and function. No new data.—I. B.

Teratoma of the PINEAL combined with adenoma (Teratom der Zirbel, kombiniert mit Adenom). Klapproth (W.), Zentralbl. f. allg. Path. u. path. Anat. (Jena), 1922, 32, 617-630; abst., Schweiz. med. Wchnschr. (Basel), 1923, 53, 299.

The physiology of the **PINEAL** gland (Beiträge zur Physiologie der Zirbeldrüse). Kolmer (W.) & Löwy (R.), Arch. f. d. ges. Physiol. (Berl.), 1922, 106, 1-14.

The pineal can be completely extirpated from rats of 30 to 50 grams weight without any after effects. Histological observations on a large number of such rats showed no trace of normal pineal gland remaining. The pineal is not necessary for life, and, contrary to Foà's results in these experiments, neither marked changes in fat formation nor earlier sexual development were observed. No macroscopic nor microscopic changes in the pineal were apparent in 4 castrated rats of 42 grams and 2 of 60 grams, 12 to 15 weeks after operation. No difference could be observed in the gland in pregnant and non-pregnant animals. Study of the nerve supply in a 3-months-old he-goat by sagittal series showed below the connective tissue envelope of the pineal a nerve fibre that, passing from the lower pole of the pineal, attached itself close to the vena magna galeni and was traceable to the tentorium. In this animal

the fibres were still non-medullated, and could therefore be easily distinguished from the fibre system of the commissura posterior or habenulae, which already was medullated. A corresponding system, in part medullated, was found in young dogs and monkeys, and, more difficultly traceable, in man. The authors name these nerve bundles "nervus conarii." They have been observed conspicuous, medullated, and with Schwann's sheath, in adult animals. Since the n. conarii is in such close union with the venous system in which are the veins of the plexus chorioidei, the possibility follows that there is in the pineal and its nerve a system influencing the circulation in the plexus and with it the secretion of fluid. This does not exclude the formation of a hormone by the pineal.—A. T. C.

Pathology and physiology of the PINEAL (*Untersuchungen zur Pathologie und Physiologie der Zirbeldrüsen*). Walter, Klin. Wchnschr. (Berl.), 1922, 1, 2401.

See Endocrin., 6, 910.

Rôle of the liver in the SECRETIN distribution in the blood (*Ueber die Rolle der Leber bei der Sekretinverteilung im Blute*). Mat-suoka (K.), Biochem. Ztschr. (Berl.), 1923, 136, 377-391.

A large series of experiments on dogs showed that the secretin content of the liver runs parallel with that of the duodenal mucosa when various diets are fed. The liver contains the most secretin when a fat diet has been fed for a long time, and the least when carbohydrates have been ingested. The liver contains a somewhat similar secretin content after prolonged fasting and after a high fat diet. The secretin content of the duodenum is dependent upon the diet. These results are taken to signify that the secretin of intestinal origin is deposited in the liver and that no hepatogenous secretin is demonstrated as dependent upon the kind of diet.

—F. S. H.

The influence of the SPLEEN on acetonuria in the dog; a contribution to the interrelationship between spleen and LIVER (*Ueber den Einfluss der Milz auf die Acetonurie beim Hunde, ein Beitrag zur Lehre von der Wechselwirkung zwischen Milz und Leber*). Gutknecht (E.), Biochem. Ztschr. (Berl.), 1923, 137, 439-449.

Diseases of the SPLEEN. Mayo (W. J.), Ann. Clin. Med. (Balt.), 1922, 1, 141-145.

The author believes that the spleen has "no important function in internal secretion."—E. C. A.

SPLENIC opotherapy of costiveness (*Opoterapia splenica e cura dalla stitichezza*). di Poggio (E.), Rassegna di clin., terap. [etc.] (Roma), 1922, 21, 194-202.

Exposition of many different clinical cases of costiveness cured by the use of a preparation of spleen, "Lienasi Sersono."—P. N.

Radiation of the SPLEEN in menorrhagia and metrorrhagia (*Unsere Milzreizbestrahlungen bei Menorrhagien und Metrorrhagien*). Scholten (G. C. J.) & Voltz (F.), *Monatschr. f. Geburtsch. u. Gynäk.* (Berl.), 1923, **62**, 194-200.

Radiation of the spleen gave relief in some 20 cases of functional hemorrhage. Treatments were given bi-weekly.—F. S. H.

The influence of the THYMUS on the SPLEEN (*Ricerche sperimentali riguardanti l'influenza del timo sulla milza*). Baggio (G.), *Arch. per le sc. med.* (Torino), 1921, **44**, 177-187.

Pathology of the THYMUS. II. Bircher (E.), *Deutsche Ztschr. f. Chir.* (Leipz.), 1922, **176**, 362-379.

Bircher's experience in Switzerland has confirmed the importance of operative reduction of the thymus to break up the vicious circle of the thymic-lymphatic status. The hospital records showed this thymic-lymphatic status in 75% to 80% of the 35 deaths in 276 cases of tetanus, diphtheria, appendicitis, and acute infectious cholecystitis. He contends that, with the mechanical factors, endocrine factors are involved in cases of "thymus death." He has operated on the thymus in 10 cases. The portions resected measured up to 10 cm. and weighed up to 45 gm. The benefit on the general condition thereafter was beyond question. The medulla always showed marked hyperplasia. He does not approve of roentgen treatment of persistent thymus or of the thyroid, regarding it as treatment in the dark, without possibility of correct dosage, while the treatment affects the whole of the thymus, and thymoprival idiocy is liable to follow. He has seen a case in which the growth was completely and permanently arrested 3 years after roentgen exposures of the thymus. In another case the exposures aggravated the symptoms so that the thymus had to be resected after all. At the operation it is easy to resect the abnormal and leave the normal portions.—*J. Am. M. Ass.*, **80**, 1186.

THYMUS in internal medicine (*Die therapeutische Bedeutung der Thymusdrüse in der inneren Medizin*). Boenheim (F.), *Deutsche med. Wchnschr.* (Berl.), 1923, **49**, 469-472.

A general review. The author recommends treatment of Graves' disease with iodine and thymus. He advocates the use of thymus for chronic ulcers of the stomach with subacidity and tuberculosis, cancer, syphilis, asthenia, etc.—J. K.

The THYMUS in young children [*Contributo allo studio anatomico e patologico del timo nella prima età. III. Le fibre a graticcio (gitterfasern)*]. Canelli (A.), *Pediatria* (Napoli), 1922, **30**, 58-64.

Case of persistent THYMUS. Chakraverti (A.), *Calcutta M. J.*, 1922, **17**, 280-282; cit., *J. Am. M. Ass.* (Chicago), 1923, **80**, 1273.

THYMIC and pseudothymic stridor (*Stridore timico e stridori pseudotimici*). Cozzolino (O.), *Boll. d. Soc. med. di Parma*, 1921, 14, 36.

See *Endocrin.*, 6, 569.

Status THYMICOLYMPHATICUS (*Zur Frage des Status thymolymphaticus*). v. Fahr (T.), *Zentralbl. f. allg. Path. u. path. Anat. (Jena)*, 1922, 32, No. 19; abst., *Schweiz. med. Wchnschr. (Basel)*, 1923, 53, 229.

(**THYMUS**) Histogenesis of Hassall's corpuscle. Cytogenetic unity of the reticular cells, the epithelial nests, the unicellular corpuscles and Hassall's corpuscles. (*Histogénèse du corpuscule de Hassall. Unité cytogénétique des cellules de charpente, des placards épithéliaux, des corpuscules unicellulaires et des corpuscules hassalliens. Contribution expérimentale*). Goldner (J.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 947-950.

Status THYMICOLYMPHATICUS in infancy. Kohlbray (C. O.), *Minnesota Med. (St. Paul)*, 1923, 6, 89-97; cit., *J. Am. M. Ass. (Chicago)*, 1923, 80, 1101.

Importance of the THYMUS in pathology (*Die pathologische Bedeutung der Thymusdrüse für den Gesamtorganismus*). Lorenz (H. E.), *Ztschr. f. ärztl. Fortbild. (Jena)*, 1922, 10, 517-522.

Some of the newer theories of the thymus are discussed. An especially good review is given of hyperplasia of the thymus, status thymicolymphaticus, the rôle attributed to the thymus in the pathogenesis of myasthenia pseudoparalytica and the theories as to the rôle of the thymus in Graves' disease.—J. K.

THYMECTOMY in infants. Marique (A.), *Arch. franco-belges de chir. (Brux.)*, 1923, 26, 127-131.

Marique has resected the thymus in 15 infants to relieve suffocation. One of the infants had 16 attacks of suffocation in one night. Through a low tracheotomy incision, he incised the capsule and shelled out as much of the two lobes as possible. He did not ligate the pedicle nor close the capsule nor suture the aponeuroses. The lips of the incision were held together with clips for two days. As soon as the infant roused from the anesthetic, the parents were allowed to take it home. If the intervention is strictly on the median line, there is no loss of blood. Most of the infants were about 3 months old, and 12 of the 15 were boys. Enough of the thymus must be left to insure ample secretion, and he asserts that the operation, under chloroform, is so simple and easy that any surgeon can undertake it without fear of mishap.—*J. Am. M. Ass.*, 80, 1345.

Five cases of THYMECTOMY (*Quinze cas de thymectomie*). Marique, *Scalpel (Brux.)*, 1922, 75, No. 50 (December 16); abst., *Presse méd. (Par.)*, 1923, 31, 87.

The rôle of the **THYROID** gland in the phenomenon of anaphylaxis (Le rôle de la glande thyroïde dans le phénomène de l'anaphylaxie). Applemans (R.), *Compt. rend. Soc. de biol. (Par.)*, 1922, **87**, 1242-1244.

Guinea-pigs were sensitized to human serum by subcutaneous injection, some before removing the thyroid, some at the time of operation, some several days after the operation. All died of anaphylactic shock when an intoxicating dose of serum was given. The conclusion is that the thyroid plays no rôle in anaphylaxis.—T. C. B.

(**THYROID**) Blepharochalasis, goiter and double lip (Das Syndrom Blepharochalasis, Struma und Doppellippe). Ascher (K. W.), *Klin. Wchnschr. (Berl.)*, 1922, **1**, 2287-2288.

A girl of 16 is described. The father had a small goiter. The girl had had a goiter since she was 4 years of age, a duplication of the mucous membrane of the upper lip and swollen upper eyelids. A man of 39 was operated upon for glaucoma. Three years later he presented a typical picture,—double mucous membrane and red, thin skin of both upper eyelids,—except that instead of a goiter, both parotid glands were swollen. The author also observed 12 cases of blepharochalasis, noting the typical duplication of the mucous membrane of the upper lip 7 times; in 4 patients the thyroid was increased in size and 3 other patients had a real goiter.

—J. K.

The relative number of leucocytes after injection of iron and **THYROID** preparations (Das relative weisse Blutbild nach Injektion von Eisen und Schilddrüsenpräparaten). Asher (L.) & Waser (A.), *Ztschr. f. Biol. (München & Berl.)*, 1920, **71**, 107-116.

Subcutaneous injections of thyroid extract and especially administration of thyroid tablets cause increase of polynuclear leucocytes with corresponding decrease of lymphocytes. The total number of leucocytes is not altered. Thyroid extract and iron preparations seem to act as an excitant upon the bone marrow. Erythrocytes remain unaltered.—A. B.

GOITER. Axtell (J. T.), *Kansas M. Soc. J. (Topeka)*, 1923, **23**, 90-92; cit., *J. Am. M. Ass. (Chicago)*, 1923, **80**, 1732.

(**THYROID**) Mongolism—Importance of early recognition and treatment. Barnes (N. P.), *Ann. Clin. Med. (Balt.)*, 1922, **1**, 302-313.

This article contains a detailed list of physical findings in mongolism. Several cases are cited of mongolism in one of twins. Inasmuch as the great majority of mongols are born to mothers near 40 years of age, the author thinks endocrine exhaustion (possibly of the thyroid or other glands) in the mother may be an important predisposing factor. An important immediate factor in the child itself may be an imperfect functioning of the thymus, with possibly imperfect function of the anterior lobe of the pituitary contributing.

Early treatment with desiccated thymus is recommended. As a prophylactic, glandular support for the expectant mother is advised. Pluriglandular preparations are condemned.—E. C. A.

(THYROID) Action of quinidin in a subject with arhythmia and with a large goiter (*Action de la quinidine dans un cas d'arythmie complète avec gros goitre*). Benhamou (E.), Paris méd., 1923, 13, 235-236.

At the time when arhythmia was treated with quinidin, the patient noticed that her goiter no longer troubled her, and even diminished rapidly in volume. She stated that the quinidin helped her goiter even more than her heart. The goiter almost disappeared. The author believes, therefore, that quinidin cured the goiter.

—R. G. H.

Technic of basal metabolism determination with demonstration of its practical application in a case of post-operative **HYPOTHYROIDISM** (*Technik der Basalstoffwechselbestimmung, mit Demonstration ihrer Anwendbarkeit an einen Fall von operativem Hypothyreoidismus*). Bircher (M. E.), Schweiz. med. Wchnschr. (Basel), 1923, 53, 143-147.

The article presents the practical application of basal metabolism, omitting the theoretical consideration. The arguments as to the relative value of the different methods are taken up. The author gives a complete description of his own apparatus which is based upon the same principal as that of Benedict. The author used his technic and apparatus in studying the changes of the basal metabolism in a young woman of 32 years who had suffered from post-operative hypothyroidism, and of a patient who was treated with dried thyroid gland substance until symptoms of the disease disappeared.—A. C. M.

(THYROID) Exophthalmic goiter after the menopause. Blamoutier (P.), Paris méd., 1922, 12, 334-338 (October 14).

The symptoms of exophthalmic goiter were accompanied with kraurosis of the vulva and intense pruritus, general at first but later limited to the genital region—all developing after the menopause in the woman of 52. Great improvement to a practical cure followed three roentgen exposures of the thyroid, and several applications of the high frequency current to the vulva, supplemented with pituitary and ovarian treatment. The pruritus subsided entirely, but still returns to a slight extent if the ovarian treatment is neglected for a few days.—J. Am. M. Ass., 79, 2040.

Nerves to the THYROID and PARATHYROID glands (*Die Nerven der Schilddrüse und der Epithelkörperchen*). Braeucker (W.), Anat. Anz. (Jena), 1922, 56, 225-249.

A detailed description of a dissection of the nerves plexuses in the neck of a 7 months' fetus with special reference to the thyroid

THYROID) Mongolian idiocy occurring in one of twins. Clay (H. T.), Arch. Pediat. (N. Y.), 1922, **30**, 726-730.

Basal metabolism. Its application to disorders of the **THYROID**. Conklin (S. D.), Atlantic M. J. (Harrisburg), 1923, **26**, 431-434.

(THYROID) Congenital myxedema (Experimentelle Untersuchungen an einem kongenitalen Myxödem). Cori (Gerty), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **25**, 150-169.

See Endocrin., **6**, 347.

Effects of irradiation of the THYROID on conception and the products of conception (Effets de l'irradiation du corps thyroïde sur la conception et les produits de la conception). Coulaud (E.), Compt. rend. Soc. de biol. (Par.), 1923, **88**, 20-21.—T. C. B.

The reticular material as an indicator of physiological reversal in secretory polarity in the THYROID cells of the guinea-pig. Cowdry (E. V.), Anat. Record (Phila.), 1922, **23**, 13 (Proc. Am. Ass. Anat.).

Primary sarcoma of the THYROID with latent pulmonary, renal and ganglionic metastases (Sarcoma primitivo della tiroide con metastasi polmonari, renali e ganglionari in un cane). Cremona (P.), N. Ercolani (Pisa), 1921, **26**, 365, 388.

Surgical treatment of HYPERTHYROIDISM. Crile (G. W.), South. M. J. (Birmingham), 1923, **16**, 459-462.

The technique of operations on the THYROID gland. Crile (G. W.) & Lower (W. E.), Surg. Gynec. & Obst. (Chicago), 1922, **34**, 258-264 (Feb.).

(THYROID) Frequency of goiters in Belgium (Étude sur la fréquence des goîtres en Belgique). Dandois, Bull. Acad. roy. de méd. de Belg. (Brux.), 1922, 5 s., **2**, 200-207.

The mechanism of melanoderma in certain HYPERTHYROID conditions (Du mécanisme de la melanodermie dans certains états hyperthyroïdiens). Delahet, Arch. de méd. et de pharm. nav. (Par.), 1921, **111**, 464-472.

The association of melanoderma with hyperthyroidism is attributed to lesions of the adrenals. Two cases are reported in which tenderness and pain are evident in the renal-adrenal region.

—F. S. H.

(THYROID) Polyarthritidis chronica deformans progressiva and Graves' disease. Deusch (G.), Klin. Wchnschr. (Berl.), 1922, **1**, 2226-2227.

The case is reported of a woman of 37. Typical Graves' disease set in when she was 14 years of age. At 19 the symptoms spon-

taneously improved and menstruation began and was quite regular. At 15 years both knee joints were swollen; this, however, disappeared. At 23 years the hand and finger joints symmetrically became stiff and typical arthritis deformans developed; she now has all the symptoms of this disease as well as of Graves' disease. The author believes this case to be a proof that arthritis deformans is due to incretory disorder.—J. K.

(**THYROID**) Recurrence of goiter (Klinische Erfahrungen bei 840 Kropfoperationen, mit besonderer Berücksichtigung der Kropf-Recidive und Recidiv-Operationen). Dubs (J.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 901-908.

Dubs relates that 6.2% of his 840 goiter operations were for recurrence. He tabulates the data from 26 cases in which paralysis of the recurrent laryngeal nerve followed the operation. He has the patient use his voice at each ligature, each clamping and each resection, and in this way was able to determine the exact cause responsible for the paralysis in all but 5 of the cases. In one patient the paralysis was bilateral, although the intervention had been on one side only. Reexamination later of 17 showed persistence of the paralysis in 11 and complete recovery in 4, with slight paralysis in 2. Recurrence of the goiter after resection was known in 55.2% of 255 cases reexamined later, and in half of the recurrence cases there were more or less serious disturbances. The interval before the recurrence developed was from 1 to 20 years; 12 years in 7 of the cases, and the interval was from 6 to 12 years in the 7 cases in which a second recurrence called for an operation. Such experiences urge the necessity for systematic iodine prophylaxis after goiter operations, at least in certain endemic foci. Conditions are much the same with goiter and with gastric ulcer; the cause still persists after excision of the lesion.—J. Am. M. Ass., 70, 1648.

Cancer **THYROIDIEN** latent avec métastase fémorale. Durand, Soc. de chir. de Lyon, 1923 (January 11); abst., Presse méd. (Par.), 1923, 31, 76.

Basal metabolism as a guide in the surgical treatment of goitre with **HYPERTHYROIDISM**. Eberts (E. M.), Canad. M. Ass. J. (Toronto), 1921, 11, 641-651.

It is held that "the basal metabolic rate is the only reliable index of the presence and degree of hyperthyroidism." The surgeon must also take into careful consideration the pulse and the condition of the heart, and especially the irritability of the nervous system. A wide margin of safety must be allowed when the nervous system bears the brunt of the intoxication. Twelve case histories are given, 7 of Graves' disease, and 5 of toxic adenoma. A chart is presented for each case showing that the basal metabolic rate in 10 cases out of 12 had fallen to normal in from 2 to 4 months.

—J. H.

Toxic Goitre. The effect of **THYROIDECTOMY** on the basal rate, the pulse rate and general nutrition. Eberts (E. M.), Canad. M. Ass. J. (Toronto), 1922, 12, 219-225.

The author reports in detail 4 thyroidectomy cases, and says that they "reflect accurately our invariable experience in 50 consecutive cases of the effect of thyroidectomy upon the basal rate, the pulse rate and the general nutrition. In no case has the procedure failed to eliminate hyperthyroidism, reduce the pulse rate to normal and restore body weight." To secure these results $\frac{3}{4}$ to $\frac{1}{2}$ of the gland must be removed and to maintain the results a prolonged period of rest after operation is essential.—J. H.

(THYROID) Hereditary myxedema. Ebright (G. E.), Med. Clin. N. Am. (Phila.), 1923, 6, 1505-1508.

Report of a case of myxedema occurring in a woman during pregnancy, who gave birth to a cretin. Thyroid opotherapy continued in the case of both mother and child for one year resulted in cure, and though both patients have to date been without treatment for 10 years, they have remained normal.—I. B.

(THYROID) Goiter prophylaxis (*Die Verhütung des Kropfes und des Kropfrecidives*). v. Eggenberger (H.), Schweiz. med. Wchnschr. (Basel), 1923, 53, 245-249.

A discussion of the present status of iodine goiter prophylaxis in Switzerland.—R. G. H.

(THYROID) The blood in myxedema. Emery (E. S.), Am. J. M. Sc. (Phila.), 1923, 165, 577-583.

A study of 14 cases leads Emery to conclude that the blood picture associated with myxedema is not constant and that there are no changes which can be cited as typical of the disease. Usually, however, there is a moderate secondary anemia. The hemoglobin is usually reduced. The white blood corpuscles average about normal but tend to vary with the red blood count. The differential count usually shows the polymorphonuclear neutrophils to be somewhat decreased in numbers. The lymphocytes may show a relative or absolute increase. There is no relationship between the degree of the anemia and the duration of the disease or the metabolic rate.

—R. G. H.

Recurrent GOITER (*Ueber Kropfrecidive*). Enderlen, München. med. Wchnschr., 1922, 69, 1129.

(THYROID) Basal metabolism. Ervin (C. E.), Atlantic M. J. (Harrisburg), 1923, 26, 429-431.

A brief review of the value of basal metabolism in its relation to thyroid disorders. Nothing new is offered.—I. B.

Graves' disease, hyperparasymphaticotonic, familial; treatment by THYROID extract (*Maladie de Basedow hyperparasymphaticoton-*

ique grave, familiale: traitement par l'extrait thyroïdien). Etienne (G.), Watrin (J.) & Richard (G.), *Rev. méd. de l'est* (Nancy), 1922, 50, 325-329; abst.; *Presse méd. (Par.)*, 1922, 30, 936.

The authors conclude that this observation demonstrates the existence among subjects with Graves' disease of predominant hyperparasympathicotonus (intense reaction to pilocarpin). It likewise shows that there are subjects with exophthalmic goiter in whom thyroid extract is indicated therapeutically. A single injection of thyroid extract, such as that recommended by Parisot and Richard for the diagnosis of thyroid disorders, by the cardiovascular reactions and the alterations of urinary and carbohydrate metabolism, indicate the proper treatment to institute. The authors consider it preferable, just as in a series of glycemia and of azotemia determinations, to utilize the thyroid extract only in brief periods; it is thus that it presents its maximum efficiency and that it is best tolerated.

—R. G. H.

"GOITER heart" and "THYMUS heart" in newly born and infants (Kropfherz und Thymusherz der Neugeborenen und Länglinge). Feer (E.), *Monatschr. f. Kinderh. (Leipz.)*, 1923, 25, 88-104.

The endemic goiter of the infant often produces an enlarged heart (dilatation with hypertrophy). This "goiter heart" is usually of toxic origin and can be cured with iodine. Hyperplasia of the thymus as well as status thymolympaticus is often complicated with slight enlargement of the heart. Often in one infant a large goiter and a large thymus are found together, thus explaining why the heart is often so large at this age. In young children it is often difficult to distinguish with x-rays between the shadow of the thymus and of the heart. Therefore, a large thymus is sometimes diagnosed as a large heart.—J. K.

(THYROID) Respiratory exchange in cretinism and Mongolian idiocy. Flemming (G. G.), *Quart. J. Med. (Oxford)*, 1922, 16, 11-21.

The basal metabolism was unduly low in the untreated cretin. Thyroid treatment raised the metabolism to about the normal level. The basal metabolism was normal in 6 Mongols. Thyroid treatment had no effect on the basal metabolism of a Mongol. Fever caused a rise in the metabolism of a Mongol. These results indicate that the basal metabolism rate referred to the body weight gives a reliable index of nutrition.—Chem. Abst., 17, 417.

(THYROID) The surgical treatment of goiter. Foss (H. L.), *Atlantic M. J. (Harrisburg)*, 1923, 26, 508-516.

This is a review of the etiology, pathology and the rationale of surgical treatment of goiter, as viewed through the medium of the author's experience. Foss is very emphatic in his statement to the

effect that with the necessary team work no mode of treatment compares with surgery in the therapeusis of goiter.—I. B.

Anemia due to THYROID dysfunction (Anaemie door dysfunctie van de schildklier). Frank (E. S.), *Nederl. Tijdschr. v. Geneesk.* (Haarlem), 1922, 66 (II), 1223-1224.

Description of a girl of 5, who was pale, but very jolly, bright and intelligent. Her face was yellow; the hair on the head was thin, the thyroid could be felt; Pirquet's test was negative. The blood contained 8,000 white and 3,350,000 red corpuscles (1-2% normoblasts).—J. K.

(THYROID) Roentgen-ray treatment of exophthalmic goiter. Fried (C.), *Deutsche Ztschr. f. Chir. (Leipz.)*, 1922, 176, 254-272.

Fried has reexamined regularly every month 13 patients with exophthalmic goiter since they were apparently cured by roentgen treatment. Both thyroid and thymus have been exposed to the rays, the dose being 80 and 91% of the erythema dose, with zinc filter. The exposure was repeated after an interval of 2 to 6 months. In one case a third exposure was given, and in 3 only a single exposure was made. The hemoglobin percentage always increased. No drugs were given, but out-door life was considered an essential element in the treatment. The women were all out-patients. Subjective improvement was noted first, but the objective signs soon followed. The exophthalmos seems to have subsided in all but one case; but in nearly all there is still a tendency to vasomotor instability and excitement, so that the patients cannot be regarded as fully recovered.—*J. Am. M. Ass.*, 80, 967.

The effect of THYROID gland from young calf upon the blood sugar in depancreatized dogs. Friedman (G. A.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1923, 20, 516-518.

Doses of adult bovine thyroid produce glycosuria in certain cases. Calves' thyroid, in contrast to the adult gland, contains no iodine. With an alcoholic extract the author demonstrated an apparent reduction in blood sugar in both normal and depancreatized animals, whether the solution was given intravenously, subcutaneously, or by mouth.—J. C. D.

The relation of the THYROID and parathyroids to pancreatic diabetes in dogs. Friedman (G. A.) & Gottesman (J.), *Proc. Soc. Exper. Biol. & Med. (N. Y.)*, 1921, 19, 215-221.

The authors outline a series of experiments on dogs. They conclude that diabetic dogs are more susceptible to tetany after partial parathyroidectomy and thyroidectomy than non-diabetic dogs after the same procedure. The removal of a thyroid in diabetic dogs seems to check the glycosuria provided tetany does not occur. If tetany does occur intravenous injections of calcium lactate may act

as a palliative in checking temporarily both the tetanic seizures and glycosuria.—J. C. D.

History and symptoms of **THYROIDISM** due to iodine administration (*Zur Geschichte und Symptomatologie der Iodothyreoidismus*). Friedman (L.), München. med. Wchnschr., 1922, 69, 1377-1378.

A patient with pyorrhea alveolaris was treated for many months with Pregl's solution, which contains iodine. A condition closely resembling hyperthyroidism developed. The author advises extreme care in the use of iodine, especially when treating patients with goiter.—J. K.

THYROIDECTOMY and immunity; **THYROID** allergy (*Thyroidectomie et immunité: allergie thyroïdienne*). Garibaldi (A.), Compt. rend. Acad. d. sc. (Par.), 1923, 176, 1341-1343.

A theoretical discussion with no new data —A. T. C

The functional relations of the **THYROID** with the other incretory glands (*Les relations fonctionnelles de la thyroïde avec les autres glandes à sécrétion interne*). Garnier (M.), J. méd. franç. (Par.), 1921, 10, 450-457.

Eclamptic tetany after **THYROIDECTOMY** (*Tétanie à forme éclamptique après thyroïdectomie*). Gaudier, Swynghedauw & Morel, Réunion méd.-chir. d. hop. de Lille, 1923, Feb. 19; abst., Presse méd. (Par.), 1923, 31, 226.

Endemic **GOITER** in lower Austria (*Der endemische Kropf in Niederösterreich*). Geringer (J.), Wien. klin. Wchnschr., 1923, 36, 186-189.

From this geographical study the author concluded that goiter is a constitutional disease frequently found in certain districts. Women are more often affected than men. Heredity also plays a rôle. Goiter is more prevalent in the higher regions than in the valleys. The cause of goiter seems to be a want of iodine in the food. Even new-born children may have goiters. The theory explaining goiter as an infection should be rejected. Ingestion of iodine as a prophylactic measure ought to be propagated by the government; this might best be accomplished by allowing only the sale of kitchen salt which contains 0.0004% iodine. It would be a valuable contribution to statistics if all cases of goiter were registered.—J. K.

Histological study of the effect of ligation of the **THYROID** vessels in exophthalmic goiter. Giordano (A. S.) & Caylor (H. D.), Surg., Gynec. & Obst. (Chicago), 1923, 35, 75; abst., Med. Sc. (Lond.), 1923, 8, 212.

The value of basal metabolic rate determinations and the **EPINE-PHRIN** test in the diagnosis and treatment of **THYROID** disor-

ders. Goetsch (E.), Long Island M. J. (Brooklyn), 1922, 16, 155-162.

The author points out that both these methods should be used. The epinephrin test may reveal cases that would be overlooked if the basal metabolism determinations alone were relied on. Moreover, the epinephrin test serves as a check on the technical errors of the other.—J. C. D.

Clinical morphological forms of GOITER (Ueber klinischmorphologische Kropfformen). Gold (E.) & Orator (V.), Wien. klin. Wchnschr., 1923, 36, 309-310.

The authors propose the following classification of goiter: (1) aplasia, including atrophy and myxedema; (2) euplasia, including the goiter of pregnancy and of school children; (3) hyperplasia, including diffuse, parenchymatous, neonatal struma; diffuse, colloid, macrofollicular struma (this last form is divided into a proliferating and a non-proliferating form); diffuse, colloid, microfollicular struma, as often seen in the mountain districts; diffuse, parenchymatous struma as in Graves' disease; and diffuse, colloid struma of exophthalmic goiter (this type is always severe and toxic); (4) hyperplastic, adenomatous forms; and (5) adenomatous forms, often with symptoms of hypothyroidism or of hyperthyroidism with symptoms of Graves' disease.—J. K.

(THYROID) X-ray and radium treatment of goiter. Grier (G. W.), Atlantic M. J. (Harrisburg), 1923, 26, 516-519.

In discussing the indications and contraindications for x-ray and radium treatment of goiter the essential prerequisite is a working classification. Grier divides his cases into goiter with hyperthyroidism, and goiter without hyperthyroidism. Subjects in the first group may be treated by radiation; those in the second group should never be so treated. The author goes into the details of the diagnosis of the types of goiter under discussion. Treatment for cosmetic effect only is not to be entertained for two reasons: first, if there is no hyperthyroidism the treatment is harmful; second, the size of the gland is usually unaffected except in hyperthyroid cases. The author advises rather mild dosage of irradiation with a treatment once a week, exposing one lobe of the gland at each sitting. The lateral lobes alone are treated; the isthmus is ignored. Each lateral area is given about one-half a skin erythema dose at each sitting, and after both lobes have been treated the patient is given a rest from treatment for 2 weeks, when the process is repeated. In this way the untoward results from x-ray treatment are avoided. The x-ray penetration corresponds to a 9-inch parallel gap, filtered through 6 mm. of aluminum. In using radium Grier employs only the gamma rays, with the radium placed 1 inch from the skin. He does not routinely expose the thymus area in cases of hyperthyroidism unless roentgenograms show that the thyroid

extends down into the chest, or that the thymus is enlarged. Hygienic and other approved measures are useful supplements in treatment. The author believes that the action of radium and roentgen rays is identical and that either may be used in a given case. If after 6 months of treatment the patient is not materially improved, surgical intervention should be considered.—I. B.

(THYROID) What types of goiter should receive medical treatment?

Guthrie (D.), *Atlantic M. J.* (Harrisburg), 1923, 26, 506-508.

In this paper the author attempts to discriminate between goiters amenable to non-surgical and those requiring surgical management. He insists that there is today much unnecessary surgery employed in the treatment of goiter. Many patients suffering from constitutional diseases but having at the same time non-toxic goiter are subjected to ill-advised operations after incomplete examinations and hasty diagnoses. Simple endemic goiter and the goiter of adolescence or pregnancy should be regarded as a deficiency disease due to lack of iodine in the organism, and amenable to prophylaxis and medical treatment. Surgery should be considered only if the case is of long standing and has resisted medical treatment. Colloid goiter should also be treated by medical measures unless pressure symptoms exist, or unless cyst formation has occurred. Malignant disease of the thyroid which can be diagnosed clinically before operation cannot be cured by surgery, as it is then too late. All sub-sternal or intrathoracic goiters are surgical cases. Non-toxic adenoma which has undergone cystic or calcareous degeneration should be treated surgically, though prior to these changes prophylactic measures are sometimes useful. Toxic adenoma is invariably a condition in which surgical methods should be employed. The acutely sick exophthalmic goiter patient is essentially a medical case, in which x-ray and radium are useful supplements. However, if the patient cannot afford the time necessary for good non-surgical response, the author advises operation. No thyroid enlargement should be operated upon until a most careful, painstaking and thorough examination is made; it is thus that unnecessary, unscientific and unwarranted surgery of the thyroid gland will be avoided.

—I. B.

(THYROID) On the amounts of enzymes in duodenal fluid in Graves' disease. Gytoku (K.), *Jap. Med. World* (Tokyo), 1922, 2, 339-343.

An examination of the duodenal fluid was made in 20 cases of Graves' disease. In 60% the enzymes were below normal in amount. No relation could be discovered between achylia or hypochlorhydria occurring in Graves' disease and duodenal enzymes. No relation was apparent between duodenal enzymes and disturbances of carbohydrate metabolism.—R. G. H.

(THYROID) A simple method for calculating the basal metabolic rate. Haden (R. L.), J. Lab. & Clin. M. (St. Louis), 1923, 8, 272-275.

Of value to the laboratory technician.—I. B.

(THYROID) Mongolism in one of twins and the etiology of mongolism. Halbertsma (T.), Am. J. Dis. Child. (Chicago), 1923, 25, 350-354.

The writer reports 5 cases.—M. B. G.

Clinical notes on hearts in **HYPERTHYROIDISM**. Hamilton (B. E.), Boston M. & S. J., 1922, 186, 216-218.

The hearts of most thyroid patients show no damage. Auricular fibrillation is the most usual type of damage, particularly in middle age or in cases of rheumatic infection. This condition is improved by digitalis and by operation.—J. C. D.

The effect of the loss of the **THYROID** and **PARATHYROID** glands at 100 days of age on the growth in body length, body weight and tail length of male and female albino rats. Hammett (F. S.), Am. J. Physiol. (Balt.), 1923, 63, 218-243.

Albino rats were used, the groups being selected from litters of 5 or more of the same sex, and each group kept in a separate cage. All were from a "gentled" colony, and weaned from the 23rd to the 28th day. The age of 100 days was selected as rats complete their period of rapid growth at about this time, according to Donaldson. The terminal point of the experiments was 150 days, when the rats were growing at the characteristic rate for the mature animal. When litters of 5 rats of the same sex were used, 2 were parathyroidectomized ("parathys"), 2 were thyro-parathyroidectomized ("thypars") and 1 was kept as control. Sexes were kept separate. The diet was the same for all. The rats were weighed and measured once a week. Qualitatively both sexes showed a retardation of growth in the parts measured. Quantitatively the females showed a greater retardation than the males, from which it would appear that females are more dependent on the stabilizing influence of the two glands than are males. Growth in body weight was inhibited more than body length and tail length, which means that cell growth by accretion is more susceptible to disturbing factors than cell growth by division. The growth capacity (increment per week ÷ wt. at beginning of week × 100) showed alternate increase and decrease in value in the "parathys," indicating repeated accumulation and subsequent elimination or destruction of toxic substances. This is not true of thyroidless rats.—T. C. B.

Surgical control of exophthalmic GOITER. Harrison (B. I.), J. Tenn. M. Ass. (Nashville), 1923, 15, 473-476; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1271.

The **THYROID** and metamorphosis (Beiträge zur biologischen Bedeutung der innersekretorischen Organe. I. Schilddrüse und

Metamorphose). Hart (C.), Arch. f. d. ges. Physiol. (Berl.), 1922, 196, 127-150.

Chiefly a theoretical discussion leading to the following conclusions: External factors of the surroundings produce a determining action on commencement and cessation of metamorphosis only by influence on thyroid function. External influences on the organism, of whatever kind (diet, climate, surroundings), act only through the intermediation of the endocrine system—A. T. C.

The influence of abnormal external temperatures on the **THYROID** and **TESTES** (Beiträge zur biologischen Bedeutung der innersekretorischen Organe. II. Der Einfluss abnormer Aussentemperaturen auf Schilddrüse und Hoden). Hart (C.), Arch. f. d. ges. Physiol. (Berl.), 1922, 196, 151-176.

House-mice, kept at 32-40° C. for some days, showed marked atrophy of the thyroid, sometimes almost complete disappearance of colloid, marked degeneration of the spermatozoa-forming epithelium, and complete cessation of spermatozoa-production in the testes. When they were kept at 4-7° C. there was increased function of thyroid, the follicles became packed with colloid, and there were marked secretion-vacuoles in the cubical epithelium, while active spermatogenesis was visible in sections of the testes—A. T. C.

(**THYROID**) A goiter family (Eine Kropffamilie). Hechinger, Klin. Wchnschr. (Berl.), 1922, 1, 1925; see also München. med. Wchnschr., 1922, 69, 1135.

A short note concerning a family of 5, all of whom developed goiter after moving from a district with little goiter to one in which goiter was frequent.—J. K.

Functional diagnosis of the **THYROID** (Zur funktionellen Schilddrüsendiagnostik). Hellwig (A.) & Neuschloss (S. M.), Klin. Wchnschr. (Berl.), 1922, 1, 1988-1992; see also p. 1128.

As a method for determining the degree of activity of the thyroid the authors recommend study of the viscosity of the blood. Before carrying out this kind of work no drugs having influence on the viscosity can be given and all diseases which may cause changes in the blood must be excluded. Increased viscosity means that there is hypofunction of the thyroid and low viscosity, hyperfunction.

—J. K.

Effect of **THYROID** treatment upon the basal metabolism in two cases of typical congenital myxedema (Effet du traitement thyroïdien sur le métabolisme basal dans deux cas de myxoedème congénital typique). Hermann (H.) & Abel (E.), Compt. rend. Soc. de biol. (Par.), 1923, 88, 93-95.—T. C. B.

THYROID therapy (Über den Jodgehalt der Schilddrüse). Herzfeld (E.) & Klinger (R.), Schweiz. med. Wchnschr. (Basel), 1922, 52, 724-727.

The comparative physiological activity of **THYROID** and **THYROXIN**. Hunt (R.), J. Pharmacol. & Exper. Therap. (Balt.), 1923, **21**, 199.

Further work on the acetonitril test for thyroid confirmed previous conclusions as to its specificity and delicacy. By this test and the effects on growth the parallelism between the iodine content of the thyroid and physiological activity has been confirmed. Physiologically "inactive" iodine was not found in any normal thyroid. Thyroxine, given by mouth or intravenously, was less active than equi-iodine doses of thyroid, as shown by the acetonitril test and by the effects on growth. The conclusion is drawn that thyroxine when given as a drug does not represent completely the physiological activity of the thyroid.—G. E. B.

(**THYROID**) X-ray treatment of goiter (*Experimenteller Beitrag zur Frage der Verwachsung nach Strumenbestrahlung*). von der Hütten (F.), München. med. Wchnschr., 1921, **68**, 983; see also, Med. Klin. (Berl.), 1921, **17**, 240.

See Endocrin., **5**, 589.

The disturbance of the **THYROID** function and the dissociation curve of oxygen of the blood. Izuka (N.), Nihon Naikagakukai Zasshi (Tokyo), 1923, **10**, 1043-1062.

In blood taken from men with disturbances of thyroid function and from rabbits either thyroidectomized or fed with thyroid, the author examined, by the use of a stalagmometer, the dissociation curve of oxygen, its variations in regard to alkali and the drop-number. With thyroid hyperfunction and hypofunction the dissociation curve of oxygen was lowered. In the latter case the curve could be elevated by the addition of a slight quantity of alkali, but this was not the case in the former. The drop-number decreased with hyperfunction, and increased with hypofunction. If the function of the thyroid was brought about to normal, all these alterations seemed to disappear. The author explained the facts found in hyperfunction as being due to some intoxication with thyroid, and those found in hypofunction as having resulted from an acidosis and an increase of the amount of fat and lipoids in the blood.—S. K.

Multiple toxic adenoma of the **THYROID**. Jackson (A. S.), Wisconsin M. J. (Milwaukee), 1923, **21**, 461-462; cit., J. Am. M. Ass. (Chicago), 1923, **80**, 1414.

Relation of the basal metabolic rate to diseases of the **THYROID** gland. Jackson (A. S.) & Jackson (R. H.), Am. J. Surg. (N. Y.), 1923, **37**, 86-90.

A general discussion illustrated by original photographs.

Therapeutic use of iodine in **GOITER** (*Ueber die therapeutische Anwendung des Iods bei Strumen*). Jagić (N.) & Spengler (G.), Wien. klin. Wchnschr., 1923, **36**, 264-265.

In most cases of goiter small doses of iodine are harmless and they are valuable in young patients with simple parenchymatous goiters. Splendid results may be obtained also in Graves' disease, although great care is necessary. When exact doses are given the body weight either remains unaltered or rises.—J. K.

The chemistry and pharmacologic action of **THYROXIN**. Kendall (E. C.), *Ann. Clin. Med. (Balt.)*, 1923, 1, 256-258.

Thyroxin acts as a catalyst. The molecule is about 65% iodine. Iodine without the nucleus is physiologically inactive. The effect of the nucleus without iodine is unknown.—*Chem. Abst.*, 17, 1282.

Influence of the **THYROID** on anaphylaxis; its administration per os a short time before the intoxicating injection (*Glande thyroïde et anaphylaxie*. Influence de la glande thyroïde sur le choc anaphylactique lors de son administration per os peu de temps avant l'injection déchaînante). Képinow (L.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 846-848.

Small doses of the gland given by mouth on the day of the intoxicating injection have no effect; the same dose given 2 days before inhibits the anaphylaxis; large doses render the animal more sensitive.—T. C. B.

Basal metabolic rate in untreated exophthalmic **GOITER**. Kessel (L.), *Tr. Am. Soc. Clin. Investigation*, 1923, April 30.

A study of the basal metabolism in 50 unselected cases of clear-cut exophthalmic goiter is reported. Forty-six records are complete and show an average initial reading of plus 44%. At the end of 3 months, 6 months and 12 months, respectively, the readings are: 3 months, 28; 6 months, 22; 12 months, 19. There is, therefore, a tendency in these patients, managed without the institution of specific therapy (spontaneous course), to a rapid, marked and progressive fall in the basal metabolism, which is accompanied by a corresponding fall in the symptoms score, in the exophthalmometer reading, in the neck circumference and by a gain in weight. Coincidentally, there is a return to economic and social utility in these patients, all of whom were confronted with great economic strain. The course of the basal metabolism should serve as a normal standard by which specific therapy may be objectively evaluated.

—*J. Am. M. Ass.*, 80, 1727.

(**THYROID**) The clinical manifestations of disturbances of the involuntary nervous system (autonomic imbalance). Kessel (L.) & Hyman (T.), *Am. J. M. Sc. (Phila.)*, 1923, 165, 513-530.

An analysis of 86 cases leads the authors to conclude, among other things, that instability of the involuntary nervous system probably constitutes a diathesis. The symptoms are strikingly similar to those in Graves' syndrome. Autonomic imbalance may coexist with myxedema. Hyperplasia of the thyroid gland is a very fre-

quent accompaniment of the syndrome. There is never present in autonomic imbalance a distinct and continuous elevation of the basal metabolism. This serves as a crucial differential point from Graves' syndrome. There are no scientific data that substantiate the participation of the ductless glands in the production of this syndrome. While patients with autonomic imbalance usually are sensitive to either atropine or adrenalin, it is possible to have the syndrome without drug sensitiveness; also it is possible without active autonomic imbalance to have drug sensitiveness. The explanation of these facts on a pharmacological basis is recorded. Clear-cut subgrouping of these patients into vagotonic and sympatheticotonic cannot be made clinically until some definite information with regard to the tonus of the involuntary nervous system is forthcoming. Autonomic imbalance can rarely be permanently arrested. Usually the symptoms may be alleviated, but the diathesis persists. Hormone therapy is without foundation, and, practically, it is useless.—R. G. H.

(THYROID) Diagnosis and roentgen-ray treatment of toxic goiter; report of five cases. Killinger (W. E.), Virginia M. Month. (Richmond), 1922, 49, 469-472 (November); cit., J. Am. M. Ass. (Chicago), 1922, 79, 2036.

GOITER in children. Klein (S.), Arch. Pediat. (N. Y.), 1922, 39, 786-799.

Ten cases are reported in which this condition was not endemic, nor very frequent. All the cases occurred in females. None gave a familial history. All but one were precocious in varying degrees. The ages of the patients ranged from 9 to 15 years in eight cases and 17 to 19 in the other two. There were 6 symmetrical thyroids and only 1 with the right lobe more prominent. There were 3 cases of hyperthyroidism, 2 with thyroid enlargement and 1 without apparent change in the gland. All had exophthalmos in varying degrees. Mentality of all was normal for the age. All 3 cases of hyperthyroidism gave a history of tonsillectomy as the beginning of their trouble.—M. B. G.

(THYROID) Recurrent goiter (Über Kropfrezidive). Klose (H.) & Hellwig (A.), Klin. Wchnschr. (Berl.), 1922, 1, 1885-1889.

Of the 167 thyroidectomized subjects examined, 40% either had a recurrent goiter or had been operated upon again. In 20.5% of these cases operation had been performed with ligation of more than 2 of the arteries; in 13% the operation had been performed on both sides, thus proving that the most extensive operation does not always bring permanent relief. The authors confirmed Roux' theory that the younger the patient the greater the possibility of recurrence. Colloid goiters are most likely of any type to recur. The recurrent goiter usually has the same histological picture as the original goiter.—J. K.

(**THYROID**) Chronic benign hyperthyroidism (Chronische gutartige Hyperthyreoidie). Konitz, München. med. Wchnschr., 1922, 69, 97.

Data reported elsewhere.—J. K.

(**THYROID**) Graves' disease; its pathogenesis and its treatment (De ziekte van Basedow, haar pathogenese en haar behandeling). Koopman (J.), Vlaamsche geneesk. Tijdschr. (Gent), 1923, 4, 2-12.

Koopman does not agree with de Stella that Graves' disease is due to thyroiditis. He believes that the pathogenesis of Graves' disease is so obscure that we scarcely know what direction investigation should take in order to find a solution of this problem.

—Author's Abst.

The **THYROID** and essential metrorrhagias (Schilddrüse und essentielle Uterusblutungen). Kräuter (R.), München. med. Wchnschr., 1922, 69, 1601-1602.

In many cases of metrorrhagia in which no local causes are detected the patient shows all or many symptoms of low thyroid activity and organotherapy with thyroid is nearly always successful, though some cases of indubitable hypothyroidism are not influenced by organotherapy. Diagnosis is often difficult; it is well to remember that the coagulation time of the blood is usually short and that the well known blood picture of Kocher is usually, though not always, found. Exact diagnosis is necessary for proper treatment.—J. K.

Description of an axolotl which, fed on **THYROID** gland, changed into an Ambystoma (Vorstellung eines Axolotls, welcher durch Fütterung mit Schilddrüse in ein Amblystoma verwandelt wurde). Krestownikoff (A. N.), Russki Physiol. J. imeni Ssetch., 1921, 3, 6-7; abst., Ber. ü. d. ges. Physiol. (Berl.), 1922, 14, 175.

Three albino axolotls received weekly 0.4 gm. each of fresh thyroid gland of a cat. Only one developed into a salamander, type Ambystoma. The other 2 died shortly after the feeding began. In all 3 it was noted that even after the ninth day there was considerable atrophy of the gills. After 3 weeks, the gill clefts and the external branchia had disappeared.—R. G. H.

Extirpation of an enormous solid tumor of the **THYROID** (Sulla estirpazione di un enorme tumore solido della Tiroide). Laccetti (C.), Ann. ital. di chir. (Napoli), 1923, 2, 290-298.

(**THYROID**) Indications for surgical intervention in toxic goiter. Langer (C.), Illinois M. J. (Oak Park), 1922, 42, 448-449. (December); cit., J. Am. M. Ass. (Chicago), 1923, 80, 208.

(**THYROID**) The Kottmann reaction (Zur Kottmannschen Jodsilbermethode). Lauda (E.), Ztschr. f. Immunitätsforsch. u. exper.

Therap. (Jena), 1922, 34, 455-472; abst., Ber. ü. d. ges. Physiol. (Berl.), 1922, 15, 314.

The serum of 3 carcinoma patients gave a positive Kottmann reaction. Its significance in thyropathies therefore needs further critical study.—R. G. H.

An unusual post-operative phenomenon in THYROIDECTOMY.
Lauddie (A. K.), Indian Med. Gaz. (Calcutta), 1922, 57, 95-96.

An enlarged right thyroid was removed in a male patient of 30. About two hours after the operation the neck was noticed to be swollen to an unusual extent. On examination the tissues were found to be edematous. There was no hemorrhage, no tachycardia, dyspnea, dysphagia, nerve pressure or other symptoms of toxic secretion. The author is unable to explain the unusual swelling.

—W. J. A.

Syphilis as a factor in THYROID and PITUITARY disease (Om lues sasom etiologiskt moment vid vissa sjukdomar i sköldkörteln och i hypophysis cerebri). Lennmalm (F.), Svenska Läk. Handl. (Stockholm), 1922, 8, 257-278.

Diseases of the thyroid and pituitary gland with following endocrine disturbances are often caused by syphilis. The author gives an extensive review of the literature on this subject. He describes 3 cases of myxedema, 1 case of exophthalmic goiter, 3 cases of acromegaly and 2 cases of dystrophia adiposogenitalis with syphilis as a probable etiologic factor.—H. B.

(THYROID) Myxedema and pregnancy (Myxoedème et grossesse).
Le Troadec (L.), Thèse de Toulouse, 1921; abst., Rev. franç. de gynéc. et d'obst. (Par.), 1923, 18, 63 (Jan.).

The author concludes that at times pregnancy in a myxedematous patient may cause disappearance or at least improvement of the myxedematous symptoms.—E. N.

(ENDOCRINE) An anatomical study contrasting the dementia precox constitution with that of paranoid developments. Lewis (N. D. C.), South. M. J. (Birmingham), 1923, 16, 327-330.

A brief digest of the author's forthcoming monograph. In addition to changes in other systems he finds the following alterations in the ductless glands. In dementia precox there was (1) regressive atrophy of the gonads, (2) atrophy of the adrenal cortex, and (3) endosclerosis and loss of colloid in the thyroid. In the paranoid cases the changes were (1) in the gonads, atrophy with areas of hyperplasia; (2) in the adrenal, widened cortex with hyperplastic areas; (3) in the thyroid, atrophy with areas of compensatory hyperplasia.—J. C. D.

Hyperesthesia of the THYROID region. Lian (C.), Bull. Soc. méd. d. hôp. (Par.), 1923, 47, 36-43.

Lian reports his further experiences with the sign described by him in 1918. It is necessary to avoid all suggestion, and to estimate the extent of hyperesthesia by merely observing the face of the patient. The point of a pin is drawn along the skin of the neck, very lightly pricking the skin. He does this on suspicion of exophthalmic goiter before he mentions the thyroid or attracts attention to it. This sign is not found very frequently, but it is reliable if it is distinctly present over the thyroid as a whole or over the isthmus or one lobe. It may be a special form of what Mackenzie calls viscerosensory reflexes.—J. Am. M. Ass., 80, 963.

The effect of **THYROIDECTOMY** on the intelligence of sheep. Liddell (H. S.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, 19, 423-425.

Twins were tested in a maze. The brighter twin was then operated upon, the other remaining as a control. It was found that cretinized sheep were inferior to the normal sheep, especially in learning a new maze.—J. C. D.

(**THYROID**) The influence of iodine on metabolism (Ueber den Einfluss des Iods auf den Stoffwechsel). Liebesny (P.), Wien. Klin. Wchnschr., 1923, 36, 154-155.

Neisser, Löwy and Zondek have described splendid results obtained in Graves' disease with very small doses of iodine. The author studied the influence of iodine on normal metabolism. He proposes the following 3 groups: (1) those in whom 2 gm. KI daily has no influence; (2) those in whom 2 gm. KI daily produces a marked rise of metabolism, without changing the pulse rate and the body weight, and (3) those in whom KI tends to diminish metabolism; in this group especially, belong patients in whom metabolism normally is rather high. The author believes that iodine therapy may be tried in Graves' disease, but only in patients under clinical control.—J. K.

THYROID gland of man during embryonal and fetal periods (Gli organi a secrezione interna nel periodo embrionale e fetale, nell'uomo. 1. Ghiandola tiroide). Livini (F.), Arch. ital. di anat. e di embriol. (Firenze), 1922, 18 (suppl.), 522-547.

A study of the development of the thyroid gland in human fetuses from 9.1 mm. and up. The article is largely morphological. The abundant blood supply and the intimate relation of the blood vessels to the epithelial cells suggest early fetal functioning.

—A. T. R.

THYROID disease. MacLean (N. J.), Canad. M. Ass. J. (Toronto), 1922, 12, 847-854 (December); cit., J. Am. M. Ass. (Chicago), 1923, 80, 208.

The effect of partial and total extirpation of the **THYROID** and **PARATHYROID** glands upon blood enzymes (Die Fermentver-

Änderung des Blutes bei vollkommener und teilweiser Entfernung des Thyreoideal- und Parathyreoidealapparates). Magath, Ztschr. f. d. ges. exper. Med. (Berl.), 1922, 29, 264-272.

The thyroid gland regulates protein metabolism in the sense that its secretion acts as a kinase for those enzymes which are concerned in the synthesis and analysis of proteins. The parathyroids regulate sugar metabolism in the sense that they furnish a kinase for amylolytic enzymes. The thyroid secretion acts as a kinase for the catalase of the cell elements.

—Chem. Abst., 17, 1048.

Case of acute exophthalmic GOITER treated successfully by use of roentgen ray. Magee (M. D'A.), Virginia M. Month. (Richmond), 1923, 50, 37-39; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1834.

(THYROID) Progressive Muskeldystrophie und Thyreohypoplasie. Maiweg (H.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. u. Leipz.), 1921, 63, 107-122; abst., Schweiz. med. Wchnschr. (Basel), 1922, 52, 1238.

Description of a case of progressive muscular dystrophy (Erb) in a 6-year-old boy manifesting typical symptoms of marked thyroid deficiency. After 6 months' treatment with thyroïdin marked improvement of both disorders was seen.—R. G. H.

(THYROID) Tachycardia with high blood pressure (Weiteres über die Hochdrucktachykardie). Mannaberg (J.), Wien. Arch. f. inn. Med., 1923, 6, 147-150.

In a previous article the author pointed out that tachycardia and hypertonia are often found together. He believed that this complication was of thyroid origin. To prove this he carried out basal metabolism determinations in 7 such subjects and found that all showed a very high basal metabolic rate.—J. K.

THYROID function. Marine (D.), Physiol. Reviews (Balt.), 1922, 2, 521-551.

Marine reviews our present knowledge of the functions of the thyroid gland. He points out that the thyroid has been shown to develop from a single ventral tubular down-growth of pharyngeal endoderm. The so-called "lateral thyroid anlagen," formerly believed to form the lateral thyroid lobes, are accidental inclusions which later undergo atrophy. A review of the literature shows that the relation between the number of mitochondrial granules and the pharmacological activity of the gland is not generally accepted in view of the abundance of these granules in the thyroid in myxedema. Thyroid adenomata are believed to develop from cell rests which atrophy under normal conditions but which form adenomata under certain conditions calling for increased thyroid activity. Thyroidectomy in animals has resulted in an average maximum reduction in total metabolism of 35% to 40%, which figure

"corresponds closely to that observed in the severest forms of human cretinism and myxedema and may be designated as the myxedema level." A close interrelationship of suprarenal cortex and thyroid has been observed, and Marine believes that exophthalmic goiter is intimately involved with cortical exhaustion and epinephrin stimulation. The review includes a survey of our present knowledge of the bearing of iodine metabolism upon the physiology of the thyroid gland and of the interrelationship of the thyroid and the other glands of internal secretion. The paper is brief and the clinician will find it well worth the reading in detail.

—Am. J. M. Sc., 165, 292.

(THYROID) Prevention and treatment of simple goiter. Marine (D.), Atlantic M. J. (Harrisburg), 1923, 26, 437-443.

An interesting and valuable review of the author's previous work on the prevention and treatment of goiter, much of which has already appeared in abstract form in this journal. Marine states that for practical purposes goiter may be divided into two great groups:

- | | | |
|----------------------------|---|---|
| | {
Endemic
Epidemic
Sporadic
"Colloid"
"Cystic" | |
| I. Simple Goiter..... | | |
| | | {
Hyperthyroidism
Toxic goiter
Toxic adenoma, etc. |
| II. Exophthalmic Goiter... | | |

Despite an enormous literature on the subject and the fact that we know more about the thyroid than any other body tissue, we know almost nothing concerning the essential nature of exophthalmic goiter. This disease occurs spontaneously only in man, while simple goiter may occur in all animals possessing a thyroid. Again, exophthalmic goiter, unlike simple goiter, is never endemic. Simple goiter may occur in any part of the world, but is less common on the sea coasts. There are occasional reports of epidemics of goiter in both man and animals. The most common endemic goiter districts are the Himalaya Mountain region of Northern India, the Alps region in Europe, the Andes plateau, and, in North America, the Great Lakes Basin and the Cascade Mountain regions of Oregon, Washington and British Columbia. The immediate cause is a deficiency in the iodine store of the thyroid. There is experimental evidence in favor of a thyroid-suprarenal cortex interrelationship. The administration of 60 to 120 mgs. of iodine in any form twice a year is sufficient to prevent simple goiter in man. Any plan of prevention that controls thyroid growths during fetal life, adolescence, and pregnancy and lactation, would practically eliminate goiter. This is not merely a question of the cosmetic appearance of the individual, but one relating also to certain dis-

eases depending upon thyroid deficiency, namely, cretinism, mutism, and idiocy. Moreover, the prevention of goiter would mean the prevention of such terminal changes as adenomata, cystic goiter, and malignancy of the thyroid.—I. B.

Possible clinical significance of THYROID-SUPRARENAL cortex interrelationship. Marine (D.) & Baumann (E. J.), N. York State J. M. (N. Y.), 1922, **22**, 518-521 (November); cit., J. Am. M. Ass. (Chicago), 1922, **79**, 2192.

(THYROID) Graves' disease treated and cured by tartar-emetic (Syndrome basedowien traité et guéri par le tartre stibié). Martin (L.), Réunion méd.-chir. d. hop. de Lille, 1923, Feb. 19; abst., Presse méd. (Par.), 1923, **31**, 226.

A subject of 40 years with Graves' disease, who would not submit to the usual treatment, was given tartar-emetic in small doses for a period of 4 months. The cure was complete and has lasted now for nearly a year.—R. G. H.

The blood supply of the THYROID gland and its surgical significance. Mastin (E. V.), Surg., Gynec. & Obst. (Chicago), 1923, **35**, 69; abst., Med. Sc. (Lond.), 1923, **8**, 212.

The THYROID gland of amphibians at the time of metamorphosis (La glande thyroïde des amphibiens au moment de la métamorphose). Mayerowna (Z.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1175-1176.

Histological description of the thyroid during different phases of metamorphosis in the tadpoles of various amphibians. The gland augments in volume considerably during metamorphosis and attains its maximum at the culminating moment of metamorphosis.

—T. C. B.

(THYROID) Idiopathic myxedema in a man of 37 (Idiopathisches Myxödem bei einem 37 jährigen Manne). Meyer-Bisch, München. med. Wchnschr., 1922, **69**, 1132.

A short note. Symptoms of myxedema began to develop when the patient was 14. Thyroid administration caused a loss of weight with an improvement of psychical functions.—J. K.

(THYROID) The treatment of goiter. McCoy (J. N.), Indianapolis M. J., 1922, **25**, 135-138.

(THYROID) Exophthalmic goiter. McGregor (J. K.), Canad. M. Ass. J. (Toronto), 1922, **12**, 860-863 (December); cit., J. Am. M. Ass. (Chicago), 1923, **80**, 208.

(THYROID) Goiter. McKechnie (R. E.), Canad. M. Ass. J. (Toronto), 1922, **12**, 854-858 (December); cit., J. Am. M. Ass. (Chicago), 1923, **80**, 208.

The basal metabolism in non-toxic goiter and in borderline **THYROID** cases, with particular reference to its bearing in differential diagnosis. Means (J. H.) & Burgess (H. W.), Arch. Int. Med. (Chicago), 1922, 30, 507-516.

Patients with an outspoken clinical picture of hyperthyroidism invariably show increased metabolism, and those with definite clinical pictures of hypothyroidism invariably show decreased metabolism. Those with goiters, but no signs or symptoms of abnormal thyroid function, for the most part show normal metabolism. The majority of patients with atypical or incomplete clinical evidence of abnormal thyroid function show normal metabolism. By inference from the indirect evidence it is believed that in these borderline cases, provided that in the first place a true basal rate is secured, and, provided that certain well recognized causes for increased metabolism, such as fever, acromegaly, leukemia and severe anemia are excluded, the finding of an increased basal metabolic rate is strong presumptive evidence of hyperthyroidism. In a similar way, provided that such conditions as starvation, hypopituitarism and hyposuprarenalism are excluded, a low metabolic rate is strong presumptive evidence of hypothyroidism. To that extent, then, the metabolism test is distinctly useful in differential diagnosis. Like all other laboratory tests it should be interpreted with due regard to all other clinical and laboratory findings, and with due regard for its limitations and pitfalls. These conclusions resulted from a study of 2,049 rate determinations on 1,000 cases, distributed as follows: clinically thyrotoxic, 300 cases; clinically myxedema and cretinism, 32 cases; goiters clinically non-toxic, 102 cases; borderline cases in which hyperthyroidism was suspected, 290 cases; borderline cases in which hypothyroidism was suspected, 70 cases; other endocrine diseases, 41 cases; blood diseases (anemia, leukemia and polycythemia), 66 cases; miscellaneous non-endocrine diseases, 99 cases.—H. L.

The rickets-producing effect of dried **THYROID**. Mellanby (E.), J. Physiol. (Lond.), 1922, 57, Proc. ii-iii.

Thyroid given by mouth has no antirachitic effect when added to a rickets-producing diet. Recent experiments show that when the diet is on the borderline, which may or may not cause slight rickets, the addition of thyroid increases the rachitic condition, although the potency of the thyroid in stimulating metabolism is evidenced by a smaller increase in weight in animals receiving it.

—T. C. B.

Chronic rheumatism from **HYPOTHYROIDISM** (Le rhumatisme chronique déformant par insuffisance thyroïdienne. Etude clinique et thérapeutique). Ménard (P.), J. de méd. et chir. prat. (Par.), 1921, 92, 134-145.

Abdominal-**THYROID** galvanization in treatment of syndrome of hyperthyroidism. Menard & Foubert, Arch. Radiol. & Electroth

(Lond.), 1922, No. 267, 143 (Oct.); cit., J. Am. M. Ass. (Chicago), 1922, 79, 2116.

The recognition of mild HYPERTHYROIDISM. Miller (J. L.) & Raulston (B. O.), Tr. Ass. Am. Physicians (Phila.), 1922, 37, 74-80.

Exophthalmos and goiter are not essential in the diagnosis of Graves' disease. The signs and symptoms of special import are tachycardia, tremor and nervousness. In every patient whose chief complaint is nervousness the possibility of hyperthyroidism should be borne in mind. We must be cautious not to overestimate the value of basal metabolism determinations as many cases of hyperthyroidism may present normal rates, and in a considerable number of instances an increased basal metabolism is due to psychic factors.—I. B.

Recognition and treatment of HYPOTHYROIDISM. Millet (J. A. P.) & Bowen (B. D.), N. York State J. M. (N. Y.), 1923, 23, 94-104.

A study is presented by Millet and Bowen of 18 cases showing either (a) myxedema, (b) clinical hypothyroidism, or (c) certain symptoms suggestive of hypothyroidism, together with a decreased basal metabolic rate and clinical improvement under thyroid therapy. The thesis is put forward that it is very difficult to classify cases falling in this third group, and to distinguish the true hypothyroid case from the case with a decreased basal metabolic rate for which hypothyroidism is not primarily responsible. Some observations are recorded as to the behavior of patients in these three groups under the different forms of thyroid therapy. It is the authors' belief that the most satisfactory type of thyroid therapy is the intravenous administration of thyroxin, controlled, where possible, by repeated estimations of the basal metabolic rate; that, further, both thyroxin and desiccated thyroid are uncertainly absorbed when taken by mouth, although either will, in most instances, bring about the desired therapeutic effect; and, finally, that for general oral administration a good preparation of desiccated thyroid is as good as, or better than thyroxin.

—J. Am. M. Ass., 80, 1177.

The value of basal metabolic studies in the differential diagnosis of conditions resembling HYPERTHYROIDISM. Presentation of four cases illustrating its value. Mohler (H. K.), Med. Clin. N. Am. (Phila.), 1923, 6, 949-959.

A discussion of the value of basal metabolism determinations in the diagnosis of borderline cases, the symptomatology of which presents many features in common. The need is emphasized for careful clinical deductions in instances in which, on final analysis, goiter is a mere incident having no bearing on the symptomatology.

—I. B.

(**THYROID**) The neotonical character of myxedema (*Über den neotenischen Charakter des Myxödems*). Moro (E.), *Monatschr. f. Kinderh.* (Leipz.), 1923, 25, 481-485.

Neotenia is the condition in which infantile characteristics remain in adults. Such symptoms in myxedema are milk teeth, retarded closing of the fontanelles, retarded ossification and persistent lanugo.—J. K.

(**THYROID**) Graves' disease with Jellineck's sign and pigmentation (*Maladie de Basedow avec signe de Jellineck et pigmentation du type addisonien; opération; disparition progressive des signes de pigmentation*). Mouriquand & Mazel, *Soc. méd. d. hôp. de Lyon*, 1922, Dec. 5; abstr., *Presse méd. (Par.)*, 1922, 30, 1078.

In 1921 the authors presented the case of a subject with Graves' disease who had, along with a state of marked malnutrition and loss of weight (10 kg. in 6 months), a very characteristic Jellineck's sign and Addisonian disturbances, especially jugal pigmentation. Although opotherapeutic treatment failed, enucleation of the parenchymatous nucleus of the thyroid improved the condition in general. The patient gained 13 kg. in weight; the symptoms of exophthalmic goiter were less marked; Jellineck's sign was considerably decreased; the pigmentation of the buccal mucosa had completely disappeared on the right; on the left, one small pale spot was slightly visible. The authors attribute these results to metabolic changes. They emphasize especially the effect on the pigmentation of the skin and the mucous membrane. If attenuation of Jellineck's sign ("thyroid sign") is easily accomplished by thyroid therapy, as has already been noted in the course of recovery in a subject with Graves' disease, the disappearance of the jugal pigmentation ("adrenal sign") deserves especial attention because it has never before been reported.—R. G. H.

Blindness in a case of **HYPOTHYROIDISM**. Improvement on treatment with glandothyrene (*Cécité par double névrite optique chez une malade atteinte d'hypothyroïdisme. Amélioration remarquable obtenue par la glandothyrene*). Mussio-Fournier (J. C.), *Ann. d'oculistique (Par.)*, 1918, 156, 265-271; see also, *Semana méd. (Buenos Aires)*, 1919, 26, 139-155.

See *Endocrinology*, 2, 526.—F. S. H.

The tadpole reaction of the **THYROID**. Naito (K.), *Rikugun Juidempo*, 1922, No. 152 (March); cit., *Jap. Med. World (Tokyo)*, 1922, 2, 274.

The relation of **THYROID** function to the blood pressure and the pulse. Nishikiro (S.), *Nihon Naikagakukai Zasshi (Tokyo)*, 1922, 10, 794-815.

Extracts of men's, cows' and rabbits' thyroids, prepared by

the author, were injected into the veins of rabbits, and the changes in the blood pressure were observed. In almost all cases the blood pressure was lowered, thereby causing a Pawlow's "Aktionspuls." Tachycardia or increased blood pressure was never found. Previous vagotomy slightly restrained the action of the thyroid extract on the blood pressure, and the "Aktionspuls" ceased to appear. The same was also found after an injection of atropin. Vagotomy carried out after an injection of thyroid extract caused an increase of the blood pressure, which was usually not the case in normal animals. Removal of the sympathetic nerves to the heart, the depressor nerve or ligature of the carotids and abdominal vessels, had no influence on the action of the thyroid extract. Thyroid extract seems to increase the action of adrenalin on blood pressure.—S. K.

(THYROID) Adenomatous goiter. Noecker (C. B.), Atlantic M. J. (Harrisburg), 1923, 26, 434-435.

Report of a case of adenomatous goiter in a woman of 50. Subtotal thyroidectomy is advocated.—I. B.

(THYROID) Colloid goiter. Noone (M. J.), Atlantic M. J. (Harrisburg), 1923, 26, 436-437.

A brief discussion of the etiology, prophylaxis and treatment of colloid goiter in which nothing new is stated.—I. B.

How does the THYROID act upon the urinary excretion of substances subcutaneously injected? Okano (Y.), Nihon Naikagakukai Zasshi (Tokyo), 1923, 10, 923-948.

If the thyroid, as Eppinger believed, provokes diuresis resulting from some alterations of the metabolism of the salts and water, it is conceivable that the thyroid may also influence the excretion (in the urine) of phenolsulphonephthalein or potassium iodid, subcutaneously injected. In order to solve this problem, the author carried out experiments on rabbits according to Eppinger's method. He examined the same rabbits to see if some variations in the rate of excretion of these substances occurred after removal of the thyroid or during thyroid feeding. On rabbits, fed on thyroid, the rate of excretion was increased. The removal of the thyroids acted in the diametrically opposite direction, although just after the operation the results were inconstant. Sometimes reverse results were found for 2-14 days after the operation, but the phenomena, owing to the decreased function of the thyroid, appeared and became more evident with time.—S. K.

The relation of the THYROID to the osmotic resistance of the red blood corpuscles. Oku (I.), Nihon Naikagakukai Zasshi (Tokyo), 1922, 10, 784-793.

The osmotic resistance and the hemoglobin content of the red blood corpuscles were examined in patients with Basedow's disease

or simple goitre. The same examination was also carried out on rabbits fed on thyroid and on rabbits after removal of the thyroid. The average value of the highest osmotic resistance and of the hemoglobin content was increased in Basedow's disease and in rabbits fed with thyroid. These results were explained by the author as due to the appearance of many newly formed red blood corpuscles in the blood stream, owing to the stimulation of the bone marrow which was probably caused by an increased function of the thyroid. In patients with simple goitre and in rabbits after removal of the thyroid, the osmotic resistance was normal, and the hemoglobin content was decreased.—S. K.

The function of the **THYROID** in hypoleucemia (*La funzione tiroidea nella leucoanemia*). Pace (L.), *Rassegna internaz. di clin. e terap.* (Napoli), 1922, 3, 521-532.

Intrafollicular hemorrhages, basophile red cells and hyperchromophile colloid of the **THYROID** body (*Recherches expérimentales sur les hémorragies intrafolliculaires les hématies basophiles et la colloïde hyperchromophile du corps thyroïde*). Parhon (C. I.) & Déréviel (M.), *Compt. rend. Soc. de biol. (Par.)*, 1923, 88, 950-951.

Amount of water in the tissues of normal and **THYROIDECTOMIZED** sheep (*Sur le teneur en eau des tissus chez les moutons normaux et thyroïdectomisés*). Parhon (Marie), *Bull. Ass. d. psychiat. Roumains*, 1922, 4, 1-4.

Analysis of blood, liver, muscles, kidneys and brain of 3 normal and 3 sheep thyroidectomized six months previously indicated that in hypothyroidism the tissues contain more than a normal amount of water.—R. G. H.

Surgery of GOITER. Pauchet (V.), *Bull. méd. (Par.)*, 1923, 37, 427-430; cit., *J. Am. Ass. (Chicago)*, 1923, 80, 1814.

(**THYROID**) Treatment of goiter (*Behandlung des Kropfes*). Payr, *Klin. Wehnschr. (Berl.)*, 1922, 1, 1862.

The author obtained good results from internal treatment of goiter. He recommends the use of protylin, but warns against internal as well as external application of iodine. Lymphocytosis is an important symptom of hyperthyroidism.—J. K.

GOITER prophylaxis (*Behandlung des Kropfes*). Payr, *Deutsche med. Wehnschr. (Berl.)*, 1922, 48, 1567.

There is a distinction between goiter as it is seen most frequently in Switzerland (*struma nodosa*) and the type of goiter most frequent in Northern Germany (*struma parenchymatosa*). The Swiss goiter usually produces hypothyreosis, the German form, hyperthyroidism. Internal treatment is advocated in the menstruation-goiter, in thyroiditis as seen after acute infectious diseases and

in hemorrhages into the parenchyma of the goiter. Operation is advocated in all cases in which the near-by organs are in any way affected. Treatment with iodine is advised only in hyperthyroidism. In hyperthyroid forms sodium phosphate often gives good results.

—J. K.

(THYROID) The surgical management of toxic goiters. Pemberton (J. de J.), Boston M. & S. J., 1922, 186, 244-254; see also, Chicago M. Rec., 44, 131-138.

An account of the methods and results obtained at the Mayo Clinic. The diagnostic and operative side of the question are dealt with.—J. C. D.

(THYROID) An epithelioma showing intercellular bridges and epithelial pearls arising in a goiter (*Sur un épithélioma à cellules à ponts et à globes cornés développé dans un goitre*). Pettit (M. A.), Bull. Acad. de méd. (Par.), 1923, 3 S., 87, 654-656.

A case report with emphasis on the pathology and origin of the neoplasm.—J. C. D.

(THYROID) The prophylaxis of endemic cretinism (*Per la profilassi della endemia gozzo-cretinica*). Pighini (G.), Difesa Sociale (Roma), 1923, 2, No. 1 (Jan.).

In the treatment of simple hypertrophy of the thyroid gland good results were obtained by the administration of iodine preparations, but in patients suffering with a severe thyroid dystrophy, Pighini was able to obtain only a partial improvement. On the contrary, good results were obtained in the treatment of goitre in subjects who drank water over a long period which had previously been boiled. The waters of countries in which endemic goitre exists have been found to be rich in carbonate salts, which are precipitated by boiling. In Talada the author noticed that the inhabitants of the country were affected with goitre. This disappeared when the inhabitants were supplied with a pure water coming from calcareous rocks. According to the author, then, the cause of goitre rests in the water. The author urges that the Italian government study carefully the problem of endemic goitre prophylaxis.—A. C. M.

(THYROID) Graves' disease produced by iodine administration during the menopause (*Über Iod-Basedow im Klimakterium*). Pineles (F.), Wien. med. Wchnschr., 1923, 73, 83-86.

The menopause is caused by loss of the endocrine function of the ovaries and by changes in other endocrine functions. It is widely believed that in this period the thyroid has an increased sensitiveness for iodine. Therefore, care in using this drug is necessary. The author describes 2 cases of simple goiter in which iodine treatment did not cause the goiter to disappear but, on the contrary, caused Graves' disease to develop. Not all women taking

iodine during the menopause, even when a goiter is present, will develop Graves' disease, but there is probably a certain predisposition to do so, due to psychical weakness or a certain liability of the involuntary nervous system.—J. K.

Results of administering iodin to patients having exophthalmic GOITER. Plummer (H. S.), Tr. Ass. Am. Physicians (Phila.), 1923, May 1-2.

It has been taught that iodine should not be administered to patients with exophthalmic goiter, on the ground that it causes hyperfunction. There are two entities included in the term hyperthyroidism: first, exophthalmic goiter; second, hyperfunctioning adenomatous goiter. In the latter, the basal metabolism is more nearly normal. In exophthalmic goiter there are certain symptoms: (1) nervous phenomena, (2) eye symptoms. The first include purposeful but useless movements. The higher psychic processes are chaotic. The patients cannot explain why they cry or laugh. In the vegetative nervous system there is the same process of imbalance. These signs have given rise to such terms as "sympathotonic" or "vagotonic" goiter. These symptoms seem to be due to underlying metabolic disturbances. Often, after slight operations, the temperature rises and death occurs in a few hours. We judge the differential diagnosis by the nervous phenomena, which, if excessive, point to a great surgical risk. The eye phenomena are two: the exophthalmos, or protrusion of the eyeball, and the stare which fluctuates with the nervous phenomena. Anything that will overstimulate the thyroid can give the clinical picture of exophthalmic goiter. In such cases, the normal hormone, thyroxine, is not completely iodized. This incompletely built up thyroxine, as it leaves the gland, can enter into catabolic reaction faster than the normal, stable molecule and raise the metabolic rate more rapidly. If, therefore, we can change the character of the molecule, we can change the basal metabolism. If there is intense metabolic stress for lack of iodine, death occurs from lack of iodine. From this it follows that if we can change the production of abnormal substance to properly iodized substance we can cut down post-operative mortality, avoid crises, and change the picture of the nervous phenomena. Acting on this plan, we administered 10 drops of compound solution of iodine for 10 days following operation, with the result that we have found there is no such thing as post-operative deaths from hyperthyroidism if this dosage has been administered to the patient with regularity. In other words, the patient is relatively short of iodine, and dies from lack of it. When we replace the iodine, we do away with post-operative deaths.

—J. Am. M. Ass., 80, 1955.

(THYROID) Goiters and their action on the blood (Zur pathologischen Physiologie der verschiedenen Kropfformen und ihrer Ein-

wirkung auf das biologische Verhalten des Blutes). de Quervain (F.), Schweiz. med. Wchnschr. (Basel), 1923, 53, 10-14.

De Quervain with Hara and Branovacky experimented on rats with the serum and thyroid tissue from 119 different cases of goiter. He used the Asher-Streuli-Duran test of the sensitiveness of hyperthyroid rats to lack of oxygen. Normal serum and the serum of cretins had no influence (in some cases the latter increased the resistance), while exophthalmic goiter acted very strongly. The thyroid acted in a similar way, and it was interesting to note that even the thyroid from cretins was not without influence. Serum from cretins to a certain extent neutralized exophthalmic goiter serum. De Quervain believes that the thyroid secretes several substances. These tests seem to prove the presence of one of them in the serum of patients.

—J. Am. M. Ass., 80, 881.

Morphology of the THYROID-THYMUS complex in the late fetal period. Histology of the thyroid and development of the arteries in the thyroid (Weitere Beiträge zur Entwicklungsgeschichte der Derivate des Kiemendarmes beim Meerschweinchen. I. Morphologie des Thyreo-thymischen Organkomplexes in der späteren Fötalperiode. II. Die Histogenese der Schilddrüse. III. Die Entwicklung der Arterien der Schilddrüse). Rabl (H.), Arch. f. mikr. Anat. (Bonn), 1922, 96, 210-314; abst., Ber. u. d. ges. Physiol. (Berl.), 1923, 17, 302.

(THYROID) Struma congenita permagna calculosa. Rauch, Deutsche med. Wchnschr. (Berl.), 1923, 49, 533.

The patient was a man of 20. At birth he had a tumor on both sides of the neck, the right tumor being hard, the left soft. During his life the tumor became very large and as hard as a bone.

—J. K.

Cholesterol: Its occurrence in two THYROID cysts: A modification of Salkowski's test. Read (B. E.) & Meleney (F. L.), China M. J. (Shanghai), 1923, 37, 236-238.

(THYROID) Clinical value of the Goetsch test. Read (J. M.) & Hiatt (R. S.), Med. Clin. N. Am. (Phila.), 1923, 6, 1527-1535.

A criticism of the epinephrin hypersensitiveness test for thyroid hyperfunction in which are included the deductions of other observers and the writers' opinions based upon tests on 59 patients with thyroid and other disorders. The authors find that this test, when positive, indicates hypersensitiveness of the sympathetic nervous system, not necessarily hyperthyroidism. Subjects of exophthalmic goiter may exhibit no hypersensitiveness to adrenalin, while frankly outspoken instances of hypothyroidism occasionally present a positive adrenalin test. Moreover, the extreme frequency with which a positive Goetsch test is encountered in cases of chronic

focal infection, menopause, and miscellaneous conditions remotely or not at all related to thyroid hyperfunction renders this diagnostic procedure the subject of a conflict of opinion "with theories of pathogenesis, not with the facts of direct observation."—I. B.

Case of lymphosarcoma of the tonsils, **THYROID** and **TESTES** (Lymphosarcome de l'amygdale, du corps thyroïde et des deux testicules). Rocher (H. L.) & Lasserre (C.), J. de méd. de Bordeaux, 1923, 95, 154-156.

THYROIDECTOMY: A modified technic. Roeder (C. A.), J. Am. M. Ass. (Chicago), 1922, 79, 2066-2068.

The surgical neuroses of the **THYROID** gland. Rogers (J.), Am. J. M. Sc. (Phila.), 1923, 165, 66-80.

The author concludes from a critical survey of available data that hypo- and hyper-thyroid conditions are interchangeable and are manifested by neuroses chiefly of the autonomic group of nerves. The hyperthyroid neuroses do not represent a primary and vicious overactivity of the gland, but seem to develop secondarily from some preceding deficiency in the biochemistry either of the involuntary nervous system or of the thyroid. The hyperthyroid symptoms are traceable to certain "hyperplastic" alveoli in the gland. When all, or the greater part, of these alveoli can be excised the symptoms quickly subside to those of the initial and underlying hypothyroidism. If the hyperplastic alveoli are scattered diffusely and evenly throughout the entire "goiter" the safest and best surgical treatment is to ligate first the two inferior thyroid arteries and later the superior vessels. The convalescence after any surgical intervention may require weeks or months of treatment with adrenal feeding and iodine to support the "check" upon the thyroid, or with thyroid feeding in the form of some "non-toxic" thyroid derivative to correct the primary hypothyroidism and to prevent its relapse into the secondary "hyper" disturbance.

—R. G. H.

THYROID disease. Roope (A. C.), J. Indiana M. Ass. (Ft. Wayne), 1923, 16, 125-129; cit., J. Am. M. Ass. (Chicago), 1923, 80, 1731.

HYPERTHYROIDISM with marked toxic symptoms due to congenital lues. Improvement with anti-luetic therapy. Rost (W.), Arch. Pediat. (N. Y.), 1922, 39, 458-461.

Case report.—M. B. G.

(**THYROID**) Trophic edema of the legs in large projecting areas accompanying a case of exophthalmic goiter (Trophœdème des jambes en vastes placards saillants et symétriques dans un cas de goitre exophtalmique). v. Sabrazes, Bull. Soc. franç. de dermat. et syph. (Par.), 1921, 28, 263-267; abst., Schweiz. med. Wehnschr. (Basel), 1922, 52, 596.

A case report of a 25-year-old girl who had had symptoms of exophthalmic goiter for the last 8 years. Three years before the report was written, after a temporary, itching, reddening condition of both legs, there developed symmetrical, painless, non-itching, sharply bounded, ashen hued, projecting solid patches, 0.5-2 cm. in size, with a smooth and here and there lightly lichen infected epidermis. This, in the present state of our knowledge, must be considered as trophic edema.—R. G. H.

(THYROID) Treatment of exophthalmic goiter (*Les traitements actuels du goitre exophtalmique*). Sainton (P.), *Vie méd. (Par.)*, 1921, 2, 1279-1282.

Relation between the THYROID and hemolysin. Sawano (T.), *Chugwai Iji-Shimpo*, 1922, No. 1018 (August); abst., *Jap. Med. World*, 2, 347.

The serum of the rabbit whose thyroid has been enucleated has an increased hemolytic effect on goat's erythrocytes. This is due to increased hemolysin. This quantitative change of the normal hemolysin can be prevented by feeding with cattle thyroid preparation, but the feeding of the normal rabbit with the same does not give any enhanced hemolysin. Moreover, when there develops intoxication phenomena from the feeding, the hemolysin contents have been found decreased. The raw cattle thyroid extracts enhance the hemolysin contents of the normal rabbit. The influence of thyroid extirpation upon the hemolysin content is not always constant and the extirpation of the organ in the immunized rabbit does not influence the immune hemolysin contents.—R. G. H.

(THYROID) Struma maligna. Schädel, *Berl. klin. Wchnschr.*, 1921, 58, 1446; see also, *München. med. Wchnschr.*, 1922, 69, 1282, 1285. See *Endocrin.*, 6, 362.

(THYROID) Peculiar murmurs in the carotid arteries (*Auffällige Gefäßgeräusche an den Karotiden*). Schipper (R.), *Wien. klin. Wchnschr.*, 1923, 36, 352.

A report of 3 cases, 2 of which are of endocrine interest. A case of hyperthyroidism was noted with a strong systolic-diastolic murmur, reaching its maximum intensity at the bifurcation of the internal and external carotid arteries. A patient with Graves' disease with murmurs in all the vessels was observed; the pulse could be auscultated.—J. K.

Difficult GOITER operations (*Schwierige Kropfoperationen*). Schloffer, *Med. Klin. (Berl.)*, 1923, 19, 446.

THYROID extirpation in tadpoles (*Ueber Schilddrüsenexstirpation bei Froschlarven*). Schulze (W.), *München. med. Wchnschr.*, 1922, 69, 1133.

See *Endocrin.*, 7, 515.

(**THYROID**) Myxedema following treatment of Graves' disease with Roentgen ray. Seymour (M.), Boston M. & S. J., 1921, 185, 261.

Two brief case reports.—J. C. D.

(**THYROID**) Exophthalmic goiter. Sheridan (L. A.), Atlantic M. J. (Harrisburg), 1923, 26, 435-436.

Report of a case of Graves' disease in a female of 19. Operation is advised.—I. B.

The **THYROID** glands of criminals sentenced to death. Shibata (I.), Kenyokwai Zasshi, 1922, No. 160 (Oct.); cit., Jap. Med. World (Tokyo), 1923, 3, 33.

(**THYROID**) Physiologic tests in the insane (Las pruebas farmacodinámicas en psiquiatría). Sierra (A. M.), Semana méd. (Buenos Aires), 1923, 30, 31-33.

Sierra reports the findings in 100 insane persons tested with the Löwi, Goetsch, Woodbury and Asoli drug tests and the Sargent and Marañon physical tests. No regular connection could be discovered between them and the mental disease. His findings demonstrate, however, that the Goetsch epinephrin test is not specific for hyperthyroidism.—J. Am. M. Ass., 80, 967.

(**THYROID**) Present status of treatment of exophthalmic goiter. Singer (K.), Med. Klin. (Berl.), 1922, 18, 1228-1229 (September 17); cit., J. Am. M. Ass. (Chicago), 1922, 79, 2200.

(**THYROID**) The indications for surgical treatment in the different types of goiter. Sistrunk (W. E.), Surg. Gynec. & Obst. (Chicago), 1921, 33, 348-352 (Oct.).

Sistrunk follows Plummer's subdivision of goiters into 3 classes: colloid, adenomatous, and exophthalmic. Colloid goiters occur in young persons, are not surgical, and respond to treatment with iodine and thyroxin. The adenomatous variety, which usually appears in young persons, show hyperthyroid symptoms in 23% of the cases. In young persons, unless the goiters produce pressure symptoms or are of considerable size, surgery is not indicated, but in patients who have reached the age of 25 or 30, surgery is advocated as a rule. All adenomatous goiters with hyperthyroidism are considered surgical if the condition of the patient will permit an operation. Exophthalmic goiters occur at any age, but most often between the ages of 20 and 40. The best treatment is surgical. Results are best when operation is performed before marked damage has been done to the vital organs. Often one or two ligations of the superior thyroid vessels, as a preliminary to thyroidectomy, make the latter safer. With proper care in the selection of the type of operation for the given case, the mortality is low.—E. N.

(THYROID) Nonthyrototoxic goiter. Slesinger (E. G.), Practitioner (Lond.), 1921, **107**, 355-366.

This is a brief review without new material.—J. C. D.

(THYROID) Relationship of goiter to chronic patient. Sloan (H. G.), Wisconsin M. J. (Milwaukee), 1922, **21**, 257-261 (December); cit., J. Am. M. Ass. (Chicago), 1923, **80**, 280.

Value of basal metabolism studies in **THYROID** disease. Smith (J. H.), Virginia M. Month. (Richmond), 1923, **49**, 708-711; cit., J. Am. M. Ass. (Chicago), 1923, **80**, 1178.

Effects of quinine therapy on the basal metabolism in the treatment of **HYPERTHYROIDISM**. Spencer (J. H.) & Lothian (N. V.), J. Roy. Army Med. Corps (Lond.), 1923, **41**, 46-47.

Administration of 40 grm. daily of quinine hydrochloride reduced the basal metabolic rate of a patient resting in bed from plus 25 to minus 14%. When out of bed his basal metabolic rate rose to minus 5%. The clinical condition was improved.—A. T. C.

(THYROID) Exophthalmic goiter; death from bilateral femoral thrombosis and gangrene. Spencer (W. G.), Brit. J. Surg. (Lond.), 1922, **9**, 568-569.

Not of endocrine interest.—J. C. D.

(THYROID) Lipodystrophia progressiva: A report of two cases, one of which showed improvement under medical treatment. Sprunt (T. P.), South. M. J. (Birmingham), 1923, **16**, 333-337.

Of endocrine interest because both subjects showed a thyroid derangement. One improved during administration of pituitary extract.—J. C. D.

(THYROID) Goiter problem—from the patient's standpoint. Starr (F. N. G.), Canad. M. Ass. J. (Toronto), 1922, **12**, 858-860 (December); cit., J. Am. M. Ass. (Chicago), 1923, **80**, 208.

(THYROID) Goiter statistics. Stoss (M.), Deutsche Ztschr. f. Chir. (Leipz.), 1922, **176**, 325-342.

Stoss analyzes 606 operative cases of goiter at Munich. In men the goiter seems to be more of an ordinary tumor type, and the disturbances are mainly mechanical, while in women the goiter seems to be more closely connected with the endocrine system, and thyrotoxic disturbances predominate.—J. Am. M. Ass., **80**, 1186.

Iodine treatment of **THYROID** diseases (Iodbehandlung der Schilddrüsenerkrankungen). Sudeck, Med. Klin. (Berl.), 1923, **19**, 449; see also, Deutsche med. Wchnschr. (Berl.), 1923, **49**, 538.

The administration of iodine in diseases of the thyroid should be considered as specific treatment. Iodine may be used in an organic or inorganic form. Iodostarin, the author states, is an or-

ganic preparation containing the hormone and can therefore take the place of the gland. This is especially useful when in severe forms the thyroid has to be completely extirpated. The body normally takes as much iodine as it needs and the rest is excreted. People in the south of Germany or in Switzerland are very sensitive to iodine. Iodine has been recently recommended in Graves' disease when given in very small quantities. The author considers this treatment as a very serious mistake. Inorganic iodine is useful only in patients in whom some active thyroid tissue is present.

—J. K.

(**THYROID**) The surgical treatment of goiter (*Die chirurgische Behandlung des Morbus Basedowii*). Sudeck (P.), *Verhandl. d. deutsch. Gessellsch. f. Chir. (Berl.)*, 1921, 45, 174-189; see also, *Arch. f. klin. Chir. (Berl.)*, 1921, 110, 648-663.

See *Endocrin.*, 6, 191.

Basal metabolism in **THYROID** disorders (*Ueber Basalstoffwechseluntersuchungen bei Schilddrüsenerkrankungen*). Szenes (A.) & Bircher (F.), *Schweiz. med. Wchnschr. (Basel)*, 1923, 53, 263-266.

A brief review with illustrative cases.—R. G. H.

Metabolic studies in diseases of the **THYROID** (*Stoffwechseluntersuchungen bei Schilddrüsenerkrankungen*). Szenes & Bircher, *Klin. Wchnschr. (Berl.)*, 1922, 1, 2597.

A cytological study on the dog's **THYROID** gland. Takagi (K.), *Folia anat. jap. (Tokyo)*, 1922, 1, 69-100.

The author has employed the cytoplasmic granular stains. He differentiates between principal, colloid, and interfollicular epithelial cells. Secretion granules are derived from plastosomes in the principal cells.—W. J. A.

The effect of **THYROIDECTOMY**, controlled by respiratory exchange measurements, on antibody formation in rabbits. Také (N. M.), *J. Infect. Dis. (Chicago)*, 1923, 32, 138-143.

Thyroid insufficiency, determined by heat production measurements, does not inhibit or increase the hemolysin and agglutinin (typhoid) formation in rabbits.—Chem. Abst., 17, 1062.

(**THYROID**) Basedow's disease. Takane (K.), *Tokyo Igakkwai Zasshi*, 36, No. 2; abst., *Jap. Med. World (Tokyo)*, 1922, 2, 237.

Goetsch test and radiotherapy in **THYROID** disease. Tarnauceanu, *J. de radiol. (Par.)*, 1922, 6, 501-511.

Tarnauceanu extols the value of the Goetsch test in hyperthyroidism. He used 1 cc. instead of 0.5 cc. of the 1:1,000 epinephrin solution. In conclusion he states that, on account of the remark-

able results, this test should be adopted as a routine practice in radiology to sift out the cases suitable for radiotherapy.

—J. Am. M. Ass., 80, 588.

HYPOTHYROIDISM with unusual skin manifestations; report of a case. Towle (H. P.) & Oliver (E. L.), Arch. Dermat. & Syph. (Chicago), 1922, N. S. 5, 88-93.

Case history and a description of the treatment used.—J. C. D.

(THYROID) Serous and endocrine glands in Malta fever (Sierose e glandole endocrine nella febbre di Malta). Tozzi (R.), Med. prat. (Napoli), 1923, 8, 1-11.

In 2 clinical and several experimental cases Malta fever produced serosites and interstitial thyroidites.—P. N.

On the function of the THYROID gland with special reference to the effect of variations of diet upon it. Part II. Tsuji (K.), Acta scholae med. univ. imp. (Kioto), 1922, 4, 471-480.

Tsuji reports a continuation of previous experiments. He found that the thyroids of rats fed on a great amount of fresh egg yolk or fresh milk present hypertrophy and activity, which produce in turn hypertrophy of the submaxillary gland, parotid gland, pancreas, liver, testicles and ovaries. The histological feature of these organs is quite analogous to that produced by thyroid feeding. On the other hand, these organs in case of thyroidectomized animals show atrophy or degeneration, the features of which are quite analogous to those found in the instances of hypothyroidism produced by the deficiency diet feeding. From these data it is concluded that fresh egg yolk or fresh milk contains a substance or substances acting hormonically on the thyroid.—R. G. H.

(THYROID) Experimental and clinical studies on the etiology and treatment of exophthalmic goitre. Tsuji (K.), Acta scholae med. univ. imp. (Kioto), 1923, 5, 329-337.

From 20 rats the entire left adrenal and $\frac{1}{2}$ - $\frac{3}{4}$ of the right were removed, leaving, however, some cortical and some medullary tissue intact in each case. Eleven rats succumbed within one day; the remainder died or were sacrificed on the second to seventh days. The thyroids and ovaries were examined. Even in this space of time the thyroid gland showed changes approaching the exophthalmic type and the ovaries showed some degree of degeneration.

—R. G. H.

The relation between THYROID function and the calcium content of organs. Uchida (R.), Nihon Naikagakukai Zasshi (Tokyo), 1923, 10, 1024-1042.

The calcium content of blood, heart, bone, liver, and kidney was determined chemically either in thyroidectomized or thyroid fed rabbits. Comparing the results with those obtained in normal rabbits, the author concludes that with hyperfunction of the thyroid

the calcium content increased in the blood, and decreased in the other three organs. The same is also found for about 5 days following thyroidectomy, while the results are quite the reverse with hypofunction.—S. K.

(THYROID) Congenital myxedema. Ugón (A. A.), Arch. latino-am. pediat. (Buenos Aires), 1922, 16, 524-528.

The child's condition improved somewhat under thyroid treatment begun when it was 11 months old. The mother, aged 38, had a goiter of 22 years' standing, and of late years had presented symptoms of hyperthyroidism.—J. Am. M. Ass., 80, 144.

The elaboration and release of the colloid of the **THYROID**. Uhlenhuth (E.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1923, 20, 494-496.

The salamander, *Amblystoma opacum*, was used. The author followed the histology of the thyroid gland throughout the life of the animal. He noted particularly that the colloid accumulates during the larval period and is discharged rapidly at the start of metamorphosis. It accumulates again in old age. He concludes from his observations and experiments in feeding iodine, that "colloid elaboration and colloid release are within certain limits independent of one another."—J. C. D.

A case of **THYROIDITIS** following parturition (Un cas d'inflammation du corps thyroïde dans les suites de couches). Vallois & Roume, Reunion Obst. et Gynéc. de Montpellier, 1922 (July); abst., Rev. franç. de gynéc. et d'obst. (Par.), 1923, 18, 57 (Jan.).

A case is reported of thyroiditis developing in a primipara of 26 on the fifteenth day after parturition. There had been a slight goiter, which became intensely inflamed, with both local and general signs. Resolution occurred, without suppuration, leaving only a slight enlargement of the thyroid.—E. N.

THYROID disorders and gestation (Maladies du corps thyroïde et gestation). Vignes (H.), J. Praticiens, 1922, 660-670 (Oct. 14); abst., Rev. franç. de gynéc. et d'obst. (Par.), 1923, 18, 101-102.

Pregnancy may improve or aggravate the symptoms of thyroid deficiency. Hypothyroidism may become a cause of vomiting, albuminuria, tetany, or even eclampsia. In general, slight insufficiency is improved; that of moderate degree is aggravated by pregnancy. The same variable effect of pregnancy is seen in the case of hyperthyroidism.—E. N.

(THYROID) A report of 150 cases of mongolian idiocy. Von Hofe (F. H.), Arch. Pediat. (N. Y.), 1922, 39, 737.

Treatment and prophylaxis of **GOITER** (Zur Therapie und Prophylaxe des Kropfes). Wagner-Jauregg (J.), Wien. klin. Wchnschr., 1923, 36, 139-142.

A discussion of the literature and a recommendation of the use of NaCl to which a trace of KI is added.—J. K.

(THYROID) Basedow's disease. Watanabe (S.), Nishin Igaku, 1922, 12, No. 4 (Dec.); abst., Jap. Med. World (Tokyo), 1923, 3, 62.

The author supports the thyroid function derangement theory but considers that the exophthalmos is of secondary importance. Thyroidectomy means the destruction of the interrelation between the primary cause, exophthalmos, internal secretion and the vegetative nervous system, while the strains of the vegetative nervous system are only accessory phenomena.—R. G. B.

Influence of radiation of the THYROID on carbohydrate metabolism. Tanemura (H.) & Watanabe (K.), Aichi Igakkwai Zasshi, 1922, 29, No. 3 (May); abst., Jap. Med World (Tokyo), 1922, 2, 265.

In normal rabbits and those with goitre, radiation caused transitory hyperglycemia, but it had no such effect on normal human subjects before or after taking thyroid extract.—R. G. B.

(THYROID) Discussion on dental sepsis as an etiological factor in disease of other organs. Willcox (W.), Proc. Roy. Soc. Med. (Lond.), 1923, 16, 16 (Sec. Odontology).

Streptococcal toxemia may result in the clinical picture of hyperthyroidism. The author has observed the disappearance of hyperthyroidism following the removal of infected tonsils in one instance, and the removal of dental sepsis in 4 others.—I. B.

(THYROID) Types of goiter and their treatment. Wilson, (J. M.), Am. J. Surg. (N. Y.), 1922, 36, 141-143.

A short discussion with case reports.—J. C. D.

Pathology of nodular (adenomatous?) goiters in patients with and those without HYPERTHYROIDISM. Wilson (L. B.), Tr. Ass. Am. Physicians (Phila.), 1922, 37, 68-73.

The parenchymal changes in the thyroid in true exophthalmic goiter is almost always diffuse, and therefore the gland is rarely nodular in appearance; "toxic adenoma," "toxic nonhyperplastic goiter," or "hyperfunctioning adenoma" is often associated with a nodular thyroid growth. In this study of about 500 thyroids the specimens were taken from two groups: (a) patients with enlarged nodular thyroids with symptoms of hyperthyroidism but without exophthalmos and without the nervous syndrome peculiar to exophthalmic goiter, but presenting a basal metabolism of plus 20 or more; and (b) patients of approximately the same age with enlarged nodular thyroids, without symptoms of hyperthyroidism and with basal metabolic rates within normal limits. In 90% of thyroids from group (a) there were distinct evidences of increased activity of the parenchymal cells, and in many instances there was

considerable parenchymal cell hyperplasia. These changes differ from those seen in the hyperplastic thyroid of exophthalmic goiter in that in most of the thyroids of the former there has been marked colloid storage in the follicles, which now is taken up by the parenchymal cells and passed into the circulation. Also, there were to be seen the peculiar picture of a mixture of hyperplastic and atrophic cells lining different parts of the same colloid-containing follicle. There were also areas of very marked formation of new follicles at times containing dense stored colloid in the encapsulated adenomas, or containing none in the nonencapsulated variety. About 95% of the thyroids examined from group (b) presented no areas of cell hypertrophy or hyperplasia; the parenchymal cells in follicles of adult type were uniformly flattened or atrophic.—I. B.

Pathologic classification of lesions of the THYROID gland. Wilson (L. B.), *Ann. Clin. Med. (Balt.)*, 1922, 1, 44-51.

A brief discussion of embryonic tissue in the thyroid, vascular changes in goiters, inflammation, hypertrophy, hyperplasia, adenomatosis, regeneration, colloid, storage, etc. Nodular thyroids due to interlobular fibrosis are often misdiagnosed as adenomas. An interesting table classifying goiters is included.—E. C. A.

Heart in exophthalmic goiter and in adenomatous goiter with HYPERTHYROIDISM. Wilson (L. B.), Boothby (W. M.) & Williams (F. A.), *Tr. Ass. Am. Physicians (Phila.)*, 1923, May, 1-2.

In exophthalmic goiter the heart work is so increased that the patient, lying in bed, needs four and five thousand calories a day. There is increased systolic blood pressure and slightly decreased diastolic pressure. In adenomatous goiter with hyperthyroidism, there is increase in both systolic and diastolic pressure. Cardiac murmurs occur in half the cases. Murmurs are of two kinds, the systolic blowing murmur, associated with changes in blood flow, and a systolic blowing murmur, with maximum at the apex, due to mitral regurgitation and enlarged left ventricle. Few patients die of heart failure in this disease. One death in 23 cases was recorded as due to cardiac failure. Difficult breathing after operation is due to anoxemia resulting from injury to the laryngeal nerve. In some patients, auricular fibrillation develops from the stress of operation. Patients with emergency operations for other conditions have developed auricular fibrillation, owing to unsuspected thyroid conditions. In our cases, sinus auricular block occurred in 1 case; T-wave negativity in 3 cases; hypertrophy in 17 cases, and fibrosis in 2 cases. Eleven of the patients were over 45, and in these lipoid changes were more marked than in other women of the same age group. The conclusions were that pronounced changes are not so frequent in goiter as is generally supposed. When they do occur, they dominate the picture; but they can be relieved greatly by proper cardiac therapy.—*J. Am. M. Ass.* 80, 1725.

Recurrent GOITER (Ueber Kropfrezidive). Wunderlich, München. med. Wchnschr., 1922, 69, 1130.

Intertracheal GOITER (Ueber Struma intertrachealis). Wurster (E.), München. med. Wchnschr., 1922, 69, 1382.

Report of an operation.—J. K.

Influence of small doses of THYROID on the red blood picture (Der Einfluss kleiner Thyreoidinmengen auf das rote Blutbild). Zondek (H.), Deutsche med. Wchnschr. (Berl.), 1922, 48, 1033-1034.

A normal woman after a severe psychic shock rapidly developed a goiter and polycythemia (14,000,000 erythrocytes, 8,000 leucocytes per mm. and 200% hemoglobin). Many members of her family suffered from thyroid diseases. X-ray treatment caused improvement. When the number of red corpuscles was 7,000,000, 0.1 gm. of thyroïdin was given. Half an hour later 15,000,000 normal corpuscles were found per mm. without abnormal cells, such as normoblasts, etc. Two hours after the injection the number of blood cells was again 7,000,000. A temporary increase of blood cells and haemoglobin may be produced in normal persons also by 0.1 gm. of threoidin. This is not due to a loss of water, as is proved by refractometric examination of the blood. Larger doses of thyreoidin have no effect or may even cause a temporary decrease of the number of red cells. In two cases of myxedema the increase after ingestion of 0.1 gm. of thyreoidin was very marked. In aplastic anemia no reaction was seen.—J. K.

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